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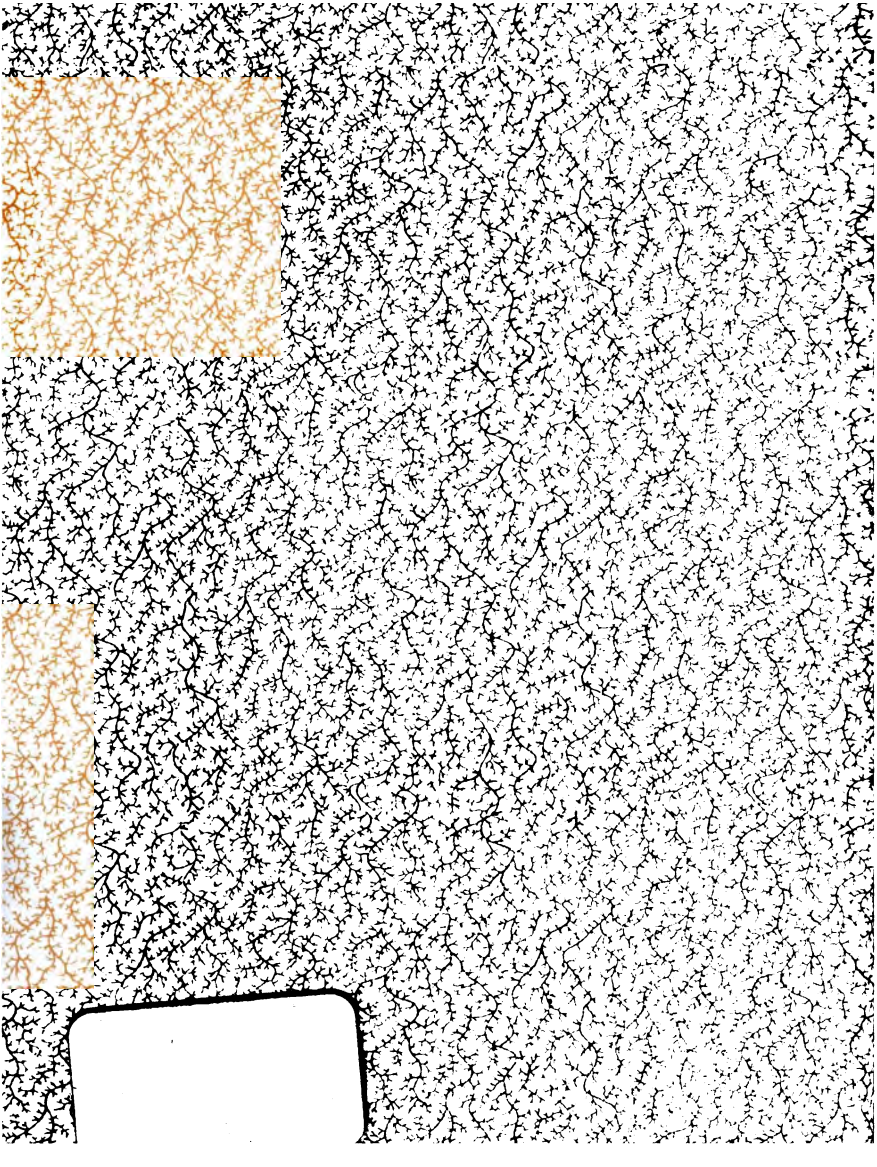

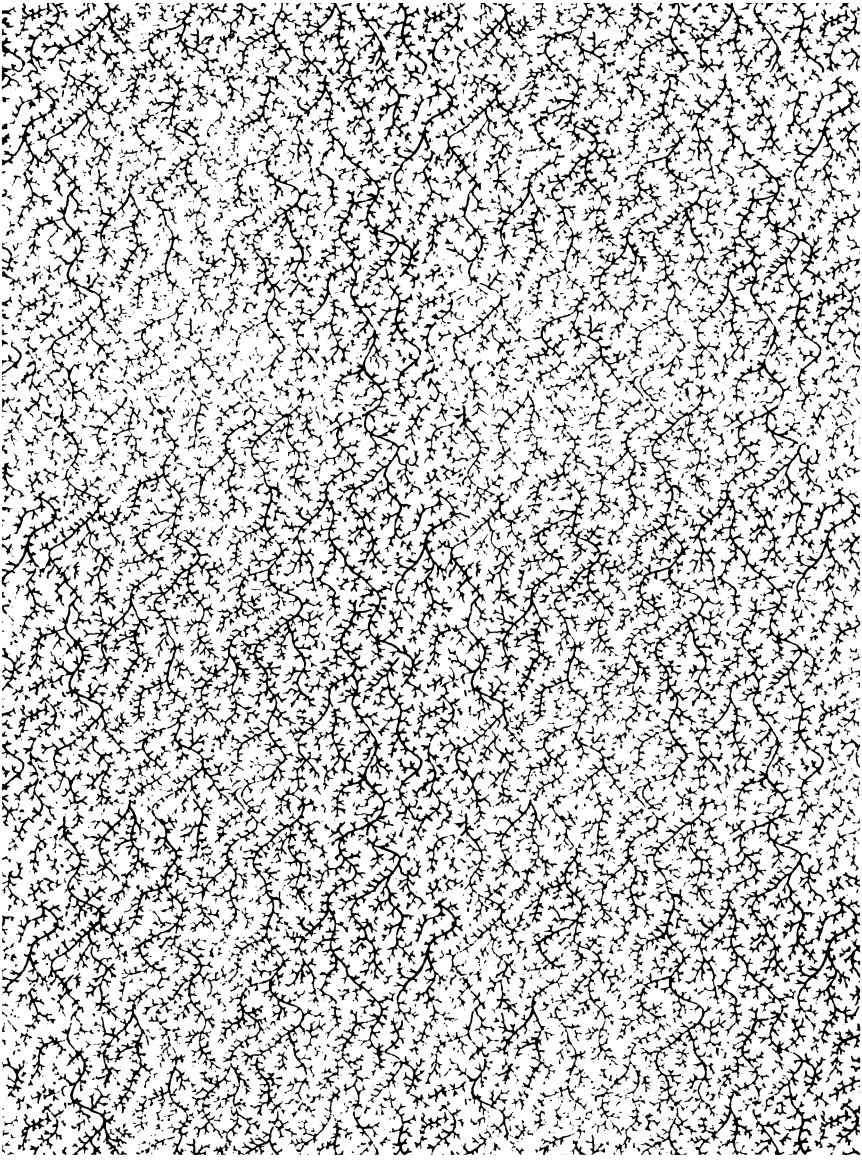

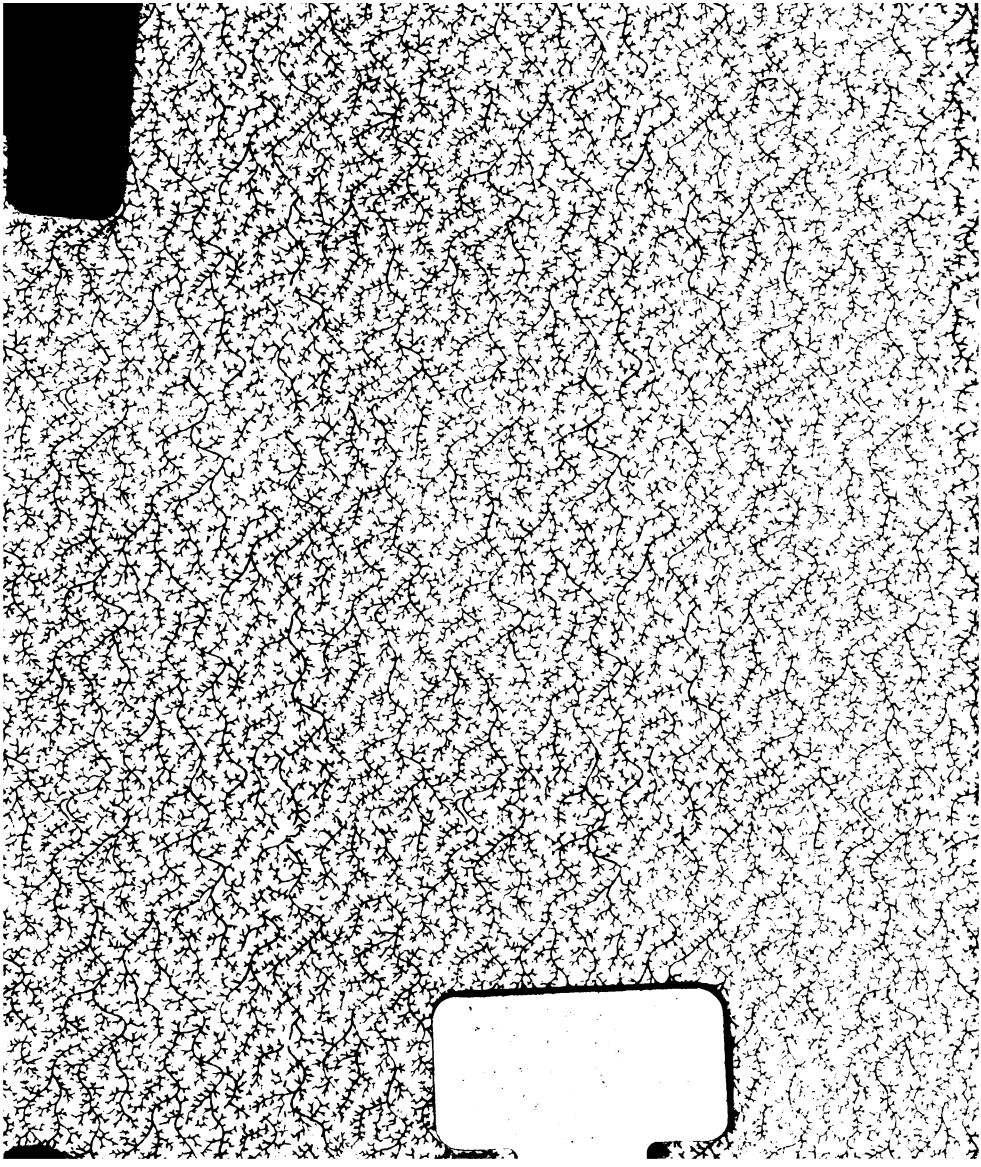

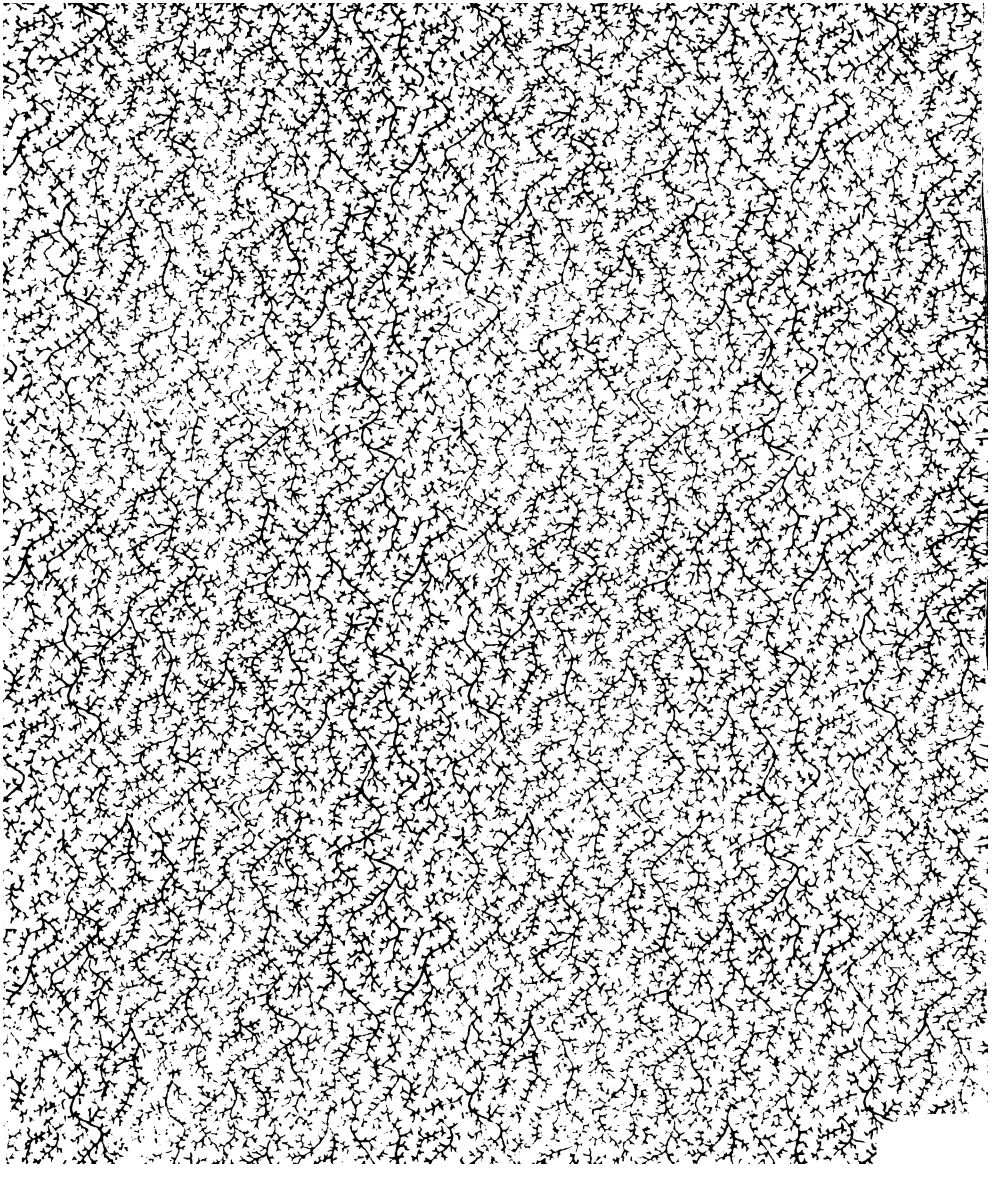

Vaccine and Serum Therapy

A Presentation of Salient Points Relating to Biologic Therapy, for the Use of Practitioners

1914
January
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Bacterial Vaccines

HISTORICAL: Metchnikoff discovered that certain leucocytes play a most important part in the process of immunity as phagocytes, by their property of taking up, destroying, and digesting pathogenic bacteria. Sir A. E. Wright, of London, demonstrated that this phagocytic power is much greater when the leucocytes are suspended in a blood serum obtained from previously immunized animals than when suspended in normal blood serum; and further, that the phagocytic power of the leucocytes is dependent upon the presence in the blood serum of certain substances having a sensitizing effect on the invading organisms. These substances were called "opsonins" by Wright, who concluded that they are naturally increased during the process of immunity; and he discovered that they may be increased by injecting bacterial vaccines.

DEFINITION: Bacterial Vaccines are suspensions in physiological salt solution of killed pathogenic bacteria. The suspensions are sterilized and accurately standardized to contain a definite number of bacteria in each cubic centimeter.

THERAPEUTIC ACTION: The therapeutic value of the bacterial vaccines is dependent upon their stimulating action on the body cells of the patient; thereby producing various antibodies—agglutinins, bacterioly-

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sins, opsonins, precipitins, and other anti-bacterial substances—and leading to a state of active immunity, which in some cases may last for a number of years.

PREPARATION: Bacterial Vaccines are prepared by the Lederle Antitoxin Laboratories from cultures of pathogenic bacteria which have been grown upon suitable media under the most favorable conditions. Several strains of the respective organisms are used; for it has been demonstrated clinically, as well as in the laboratory, that different cultures of the same organism may vary widely in biochemic properties; and that most vaccines should be polyvalent in order to possess the greatest efficiency. Polyvalent means that the suspension contains several cultures of the same species of bacteria —that is, several "strains of the organism are used—the cultures being obtained from many different sources of infection in which that species of organism is found. All of the bacterial vaccines prepared in the Lederle Antitoxin Laboratories are polyvalent—the single as well as the combined (mixed) vaccines. This statement, however, is not applicable to Typhoid Vaccine, in which only one strain of the typhoid bacillus is used; because this particular strain has proved to be most efficient in the use of Typhoid Vaccine in the United States Army and in the armies of other countries. A combined (mixed) vaccine contains the various species of bacteria generally present in a mixed infection: for example, Pneumococcus

Combined Vaccine (Mixed) contains the pneumococcus, streptococcus, and staphylococcus.

The bacterial cultures, which are usually grown on some solid medium, are washed off with physiological salt solution, and thoroughly shaken to separate the organisms: the bacterial suspension is subjected to a careful count: the organisms are killed by heating the suspension and by the addition, after cooling, of 0.25% trikresol. The suspension is then diluted with sterile physiological salt solution, containing 0.25% trikresol, until each cubic centimeter contains the desired number of bacteria.

USES: Bacterial Vaccines are used in acute, subacute, and chronic infections. Their therapeutic value can no longer be questioned: they are not, of course, panaceas; but they do produce brilliant results when intelligently employed.

DIAGNOSIS: In certain diseases, it is desirable that an accurate bacteriological examination be made; for, since each bacterial vaccine exerts a specific action, the one to be selected for use in any given case should correspond to the predominating type of organism causing the infection. However, it is not always practicable for such an examination to be carried out; and in most cases a correct diagnosis may be made from the clinical symptoms. But if the disease does not readily yield to

the treatment, a bacteriological examination should then be made if possible; and this examination is particularly valuable in determining the existence and nature of mixed infections.

Since a very large majority of diseases are due to mixed infections, the combined (mixed) bacterial vaccines have been prepared for treating such cases. These combined (mixed) vaccines contain combinations of those organisms which have been found most frequently associated in producing or aggravating such diseased conditions. Very often, where treatment with a single vaccine produces little or no result, the use of a combined (mixed) vaccine is followed by very striking and positive results.

METHOD OF ADMINISTRATION: Bacterial Vaccines are administered subcutaneously by using the Lederle Syringe container, or by means of an ordinary hypodermic syringe; in the latter case, the required amount of vaccine is withdrawn into the hypodermic syringe from the Lederle Vial. If the ordinary hypodermic syringe is used, the instrument must be properly sterilized, preferably by boiling; or by repeatedly washing it out with 5% phenol solution—the needle must also be cleansed internally and externally by the same means —and the instrument should finally be rinsed out with boiled water. The Lederle Syringe is aseptic and ready for immediate use.

The injections may be made in the scapular region; in the arm at the insertion of the deltoid muscle; in the gluteal region; in the abdominal wall—in short, at any point where there is sufficient subcutaneous tissue; preference being given to the region in which the injection will produce the least pain or discomfort. At the point of injection, the skin may be painted with iodine, or cleansed with soap and water and mopped with alcohol. Any air contained in the syringe should be expelled before injecting the vaccine. After the operation, the site of injection may be protected with a sterile gauze dressing, or may be wiped with a pledget of cotton moistened with alcohol.

The container—whether it be the Syringe or the Vial—should be well shaken before using the vaccine, in order to suspend any bacteria that may have settled out on standing.

DOSAGE: Theoretically, the opsonic index of the blood is a valuable guide in determining the size and frequency of the dose of the vaccine; but the process of estimating the opsonic index is so intricate, so tedious, and so liable to error that it is not practicable in general. In practice, therefore, the clinical symptoms—temperature, pulse, amount of pain, degree of swelling and inflammatory reaction in local infections, and the patient's general condition—may be safely relied upon in determining the amount and interval of the doses. The gen-

eral rule is to begin with small doses and progressively increase; immunity being more effectively produced by repeated injections of gradually increasing doses, than by a single injection of a large dose. At the same time, the clinical effects in the individual case must be made the basis for the size and frequency of the doses; for the dosage is influenced by the nature of the infection, and also by the individual susceptibility. Should no improvement be noted, the size of the dose may be increased, or the intervals shortened, or both. If a pronounced clinical reaction occurs—characterized by general malaise, fever and aggravation of local symptoms—it indicates that the dose has been too large; and the next injection should be smaller.

The amount of vaccine required varies according to the age and personal characteristics of the patient; the type, duration, extent, and severity of the infection; and the identity of the organisms. When the general condition of the patient is good, the response to the vaccine is more effective; hence, it may be necessary to administer the vaccine every 24 hours or oftener to an extremely ill person, while every five days might suffice for one who is convalescent.

As a general rule, the intervals between the doses in acute infections vary from one to two days. After the acute symptoms have subsided—as shown by a drop in the temperature and by other signs of improvement—the intervals may vary from two to five days. In sub-

acute and chronic infections, the vaccine should be given every three to seven days; the doses being increased according to the clinical symptoms.

Antibacterial Serums

SERUMS VS. VACCINES: Immune sera are fluids containing antibodies already formed, and are injected into the circulation to supply antibacterial elements without stimulating the body cells to the production of these substances. Hence, in the use of sera, the antibodies formed by the body cells of the horse or other animal are supplied to the patient; and a condition of passive immunity is established, lasting only a few weeks. Therefore, sera differ from bacterial vaccines: the latter confer active immunity which in some cases may last for a number of years. Moreover, bacterial vaccines do not contain antibodies; their therapeutic value depends upon their stimulating action on the body cells of the patient, thereby producing various antibodies.

It requires an appreciable amount of time for antibodies to be formed after injection of bacterial vaccines. Therefore, an immediate immunity does not follow; but, after it is established, the immunity persists for a long period. Thus, the immunity against typhoid fever —induced by TYPHOID VACCINE (PROPHYLACTIC)—is not easily demonstrated until several days after the injection, and does not apparently reach its maximum intensity until at least 10 days after the injec-

tion of the vaccine. It is probable, however, that the formation of immune bodies begins very shortly after the injection is made. On the other hand, the immunity conferred by an antitoxic or an antibacterial serum begins at once: If the serum is injected intravenously, the entire content of immune bodies is at once available; if the serum is injected subcutaneously or intramuscularly, the immune bodies are available as rapidly as the serum is absorbed. As soon as the serum reaches the circulation, the process of elimination is begun and proceeds rapidly; so that, within a few days, the demonstration of immune bodies is difficult.

DEFINITION: Sera containing substances which result in the death and destruction of bacteria are called Antibacterial Serums. Acquired antibacterial immunity depends on the destruction of bacteria before they have had sufficient opportunity to multiply and produce poisons which kill the body cells. Various kinds of antibodies are found in the sera of animals that have acquired antibacterial immunity: the best known of these antibodies are bacteriolysins, opsonins, agglutinins, and precipitins. These prepared antibodies are introduced into the system of the individual by the injection of Antibacterial Serums, which produce a condition of passive immunity.

IMMUNE SERA: There are two varieties of immune sera: (1) Antitoxic Serums and (2) Antibacterial Serums. The former—represented by Diphtheria Anti-

toxin and Tetanus Antitoxin—neutralize the toxin in the circulation and in the various tissues and body cavities. In diphtheria and tetanus, the bacteria elaborate a poison or toxin which is absorbed into the circulating blood and is carried to the tissue cells; and this toxin must be rendered inert in order to effect a cure of the disease. The Antibacterial Serums, however, act directly upon the invading organisms and render them inert or destroy them; thereby arresting the disease.

ANTIBACTERIAL VS. ANTITOXIC SERUMS: Immune sera contain antibodies already formed: these antibodies in the Antitoxic Serums are chiefly antitoxins —substances which neutralize the bacterial poisons or toxins; while in the Antibacterial Serums, the antibodies consist of bacteriolysins, agglutinins, precipitins, opsonins, and other substances—all of which act directly upon the bacteria and tend to destroy them and their intracellular products.

USES: The practical application of specific Antibacterial Serums, in the treatment of various infections in man, has been used on a large scale. It has been found that by the early injection of serum from animals actively immunized to various organisms, the natural resistance of infected individuals can be augmented and the course of the disease materially ameliorated and shortened. Even in desperate cases, injections of large quantities of Antibacterial Serums have yielded most

unexpectedly favorable results; while small doses, in similar cases, have usually been without beneficial action.

Antibacterial Serums are preferably used when the disease is severe, and the patient's resistance is low. Bacterial Vaccines are also used in severe cases; but beneficial effects cannot be expected in as short a time from the use of Bacterial Vaccines as from Antibacterial Serums, since the latter contain antibodies already formed; while in the use of Bacterial Vaccines, the body cells of the patient must first be acted upon, and stimulated to the production of antibodies. This is necessarily a biologic process consuming a definite period of time, and in some cases it appears to be almost impossible to stimulate the body cells to the production of antibodies.

CONJOINT USE OF VACCINES AND SERUMS: If treatment is begun with the serum, immune bodies are at once furnished; but, being contained in a foreign protein, they are rapidly eliminated, and in a few days only a trace of immune bodies can be detected. In order to establish a permanent immunity, a vaccine may be used, and, if injected at about the same time as the serum, will stimulate the body cells of the patient to the production of antibodies which will maintain the immunity; so that the patient will be protected after the antibodies in the injected serum are eliminated.

THERAPEUTIC VALUE: The results of Antibacterial Serums in the treatment of diseases of man

have, however, not always been as satisfactory as those obtained with specific Antitoxin Serums. The chief reasons for failure are:

(1) It is not possible to accumulate, in the serum of immunized animals, antibacterial elements in concentration which is at all comparable to the concentration of antitoxins in Antitoxic Serums.

(2) It has been impossible to adjust the dosage by any accurate unit of antibacterial elements and the doses which have generally been used have doubtless been too small to produce the desired favorable results.

STANDARDIZATION: Up to the present time, no universally accepted unit of immunity has been applied to the Antibacterial Serums. However, in the Lederle Antitoxin Laboratories, the therapeutic activity and antibody content of the serum obtained from each immunized horse are determined as accurately as possible by certain laboratory methods: including the estimation of the opsonic index, the complement fixation test, and similar immune serum tests. The serum is also subjected to the most careful and rigid bacteriologic and physiologic tests, in order to establish its safety.

PREPARATION: Antibacterial Serums are obtained from the blood of horses that have been immunized by injecting gradually increasing doses of a vaccine and an autolysate made from cultures of the specific micro-organisms; inoculations of vaccine and

autolysate being made at frequent intervals. Many different strains of the bacteria are used in preparing the vaccine and the autolysate for inoculation. The vaccines are made in the same manner as used for Bacterial Vaccines. In preparing the autolysates, the live bacteria are suspended in distilled water and allowed to extract for a week at ice-box temperature (40° F.); after which sodium chloride is added to nine-tenths of one per cent. before inoculation.

DISEASES

in which

Prophylaxis and Treatment by Vaccines and Serums have been successfully employed

With the Dosage of each product

Acne

ACNE VULGARIS is probably one of the most trying, as well as one of the most numerous, conditions which the physician is called upon to treat. Acne may be divided into two classes: the non-pustular variety, in which comedones are the predominating lesions; and the pustular type. The acne bacillus is the direct cause of all cases of acne. In the pustular variety of this disease, the staphylococcus is the chief complicating infective agent.

ACNE VACCINE is employed in the treatment of non-pustular acne vulgaris, in which the predominating lesions are comedones. Vaccine therapy is not in itself sufficient to correct this condition; but, when combined with proper hygienic and surgical measures, excellent results are obtained. Local treatment of the skin should not be neglected. All pustules should be wiped with alcohol and incised, and comedones should be expressed.

ACNE COMBINED VACCINE has proved to be a most useful adjunct in the treatment of pustular acne. The vaccine treatment should be preceded by surgical measures: namely, the pustules should be wiped with alcohol and then incised.

DOSAGE: The initial dose of ACNE VACCINE should not exceed 5 million; the best results being ob-

tained with initial doses of 3 to 5 million. Subsequent doses may be gradually increased, but most dermatologists advise the continued use of small doses—ranging from 5 to 30 million. The initial dose of ACNE COMBINED VACCINE (Mixed) should not exceed 55 million, and subsequent doses may be increased as indicated by the clinical symptoms.

If new lesions appear 3 days after injection of the vaccine, it is an indication that the dose was too large. It is recommended that the doses be administered at intervals of 4 or 5 days.

QUANTITY IN CONTAINER: Acne vaccines include Acne Vaccine and Acne Combined Vaccine (Mixed). Acne Vaccine is supplied in dilutions of 5 million, 10 million, 20 million, 40 million, and (in syringes only) 100 million. Acne Combined Vaccine (Mixed) is supplied in five dilutions; the No. 5 being marketed in syringes only.

No. 1 contains	5 million B. Acne. 50 million Staphylococci (albus and aureus).
No. 2 contains	10 million B. Acne. 100 million Staphylococci (albus and aureus).
No. 3 contains	20 million B. Acne. 200 million Staphylococci (albus and aureus).

No. 4 contains 40 million B. Acne.
400 million Staphylococci (albus and aureus).

No. 5 contains 100 million B. Acne.
1000 million Staphylococci (albus and aureus).

PREPARATION: Several strains of the Bacillus Acne—isolated from cases of acne vulgaris—are grown anaerobically on oleic acid-dextrose agar. The vaccine is prepared from the cultures in the manner described on page 12.

Acne Combined Vaccine is prepared by mixing separate vaccines of the various bacteria mentioned above.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Boils, Carbuncles, Sycosis, Eczema, etc.

In no class of diseases has the use of Bacterial Vaccines been more thoroughly effective than in the various dermatoses. Some of the earliest work in this interesting field of research has been in this specialty. This undoubtedly is due to the fact that infections of the skin are so common; also that the infecting organism is so easily procured and the results of the treatment so read-

ily observed. Since the staphylococcus is normally present on the skin, it would naturally be considered as being either the primary cause or the complicating factor in most skin diseases. Because of this fact, STAPHYLOCOCCUS VACCINES have been extensively employed and are of great value in the treatment of a large variety of cases, especially in furunculosis, sycosis, acne, certain form of eczema, pustular rosacea and impetigo; excellent results are also obtained in fistulous sinuses, psoas abscess, cystitis, otitis media, suppurating glands, osteomyelitis, and septic infections. As a rule, in using STAPHYLOCOCCUS VACCINES, the acute inflammation and pain begins to subside within 24 hours after the first inoculation. If necrotic tissue, or pus, has been formed before the vaccine was used, the abscess should be incised; but where the vaccine is given early, almost invariably the inflammatory process will subside without pus formation. This point is very clearly illustrated in cases where furunculosis exists in various stages of development at the time when the vaccine is given. Some surgeons are employing STAPHYLOCOCCUS COMBINED VACCINE before abdominal operations as a preventative for post-operative infection. STAPHYLOCOCCUS-STREP VACCINE is used in suppurative periostitis, osteomyelitis, pleurisy, peritonitis and various pyemic conditions.

DOSAGE: Initial doses of 50 million to 100 million of STAPHYLOCOCCUS ALBUS VACCINE,

STAPHYLOCOCCUS AUREUS VACCINE, or STAPHYLOCOCCUS VACCINE (albus, aureus and citreus) are advisable. It has been demonstrated that the best results are obtained when the first dose of these vaccines is small. If a pronounced clinical reaction occurs, the dose should not be increased! The best plan is to begin with a dose of 50 million: after 4 or 5 days inject 100 million; and gradually increase the dose every 4 or 5 days.

STAPHYLOCOCCUS COMBINED VACCINE (Mixed) is given in doses of 175 million to 1,400 million; the former being the average dose, while the latter is used in profound toxemia, puerperal sepsis, etc.

The initial dose of STAPHYLOCOCCUS-STREP VACCINE varies from 75 to 125 million, subsequent doses being increased at 3 or 4 day intervals according to clinical manifestations.

QUANTITY IN CONTAINERS: Staphylococcus vaccines include five varieties: (1) Staphylococcus Albus Vaccine; (2) Staphylococcus Aureus Vaccine; (3) Staphylococcus Vaccine (albus, aureus and citreus); (4) Staphylococcus Combine Vaccine (Mixed), containing Staphylococci (albus, aureus, and citreus); Streptococci; and Bacilli coli communis; and (5) Staphylococcus-Strep Vaccine, containing Staphylococci (albus and aureus) and Streptococci.

Staphylococcus Albus Vaccine, Staphylococcus Aureus Vaccine, and Staphylococcus Vaccine (albus, au-

reus, and citreus) are supplied in dilutions of 250 million, 500 million, 1,000 million and 2,000 million. The Staphylococcus Combined Vaccine (Mixed) is supplied in five dilutions; the No. 5 being marketed in syringes only.

No. 1 contains 100 million Staphylococci (albus, aureus, and citreus mixed).
25 million Streptococci.
50 million B. coli communis.

No. 2 contains 200 million Staphylococci (albus, aureus, and citreus mixed).
50 million Streptococci
100 million B. coli communis.

No. 3 contains 400 million Staphylococci (albus, aureus, and citreus mixed).
100 million Streptococci.
200 million B. coli communis.

No. 4 contains 800 million Staphylococci (albus, aureus, and citreus mixed).
200 million Streptococci.
400 million B. coli communis.

No. 5 contains 1600 million Staphylococci (albus, aureus, and citreus mixed).
400 million Streptococci.
800 million B. coli communis.

Staphylococcus-Strep Vaccine is supplied in four dilutions:

No. 1 contains 100 million Staphylococci (albus and aureus).
25 million Streptococci.

No. 2 contains 200 million Staphylococci (albus and aureus).
50 million Streptococci.

No. 3 contains 400 million Staphylococci (albus and aureus).
100 million Streptococci.

No. 4 contains 800 million Staphylococci (albus and aureus).
200 million Streptococci.

PREPARATION: Staphylococcus Vaccines are prepared after the manner described on page 12, using cultures of the organisms mentioned above.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Colds, Influenza, etc.

The results of bacteriological examination, by various investigators, of the secretions of individuals suffering from COLDS and other CATARRHAL CONDITIONS OF THE RESPIRATORY TRACT, have revealed the fact that these affections are caused chiefly by bacteria which are almost constantly present during health. Certain external influences—such as exposure to drafts—lower the resistance of the mucous membrane to such an extent that the natural forces can no longer hold in check the bacterial growth; and the increased secretions form a suitable medium in which the organisms may rapidly grow. The most common, persistently pathogenic of these organisms are the micrococcus catarrhalis, the influenza bacillus, the Friedlander bacillus, the pneumococcus, the streptococcus and the staphylococcus.

Among the most common ailments met with in general practice are those due to, or associated with, the in-

fective processes of the upper respiratory tract. CORYZA, or common COLDS, and INFLUENZA respond readily to vaccine therapy. Catarrhs are so liable to become chronic under conventional treatment that the early use of Bacterial Vaccines becomes an important factor. When the vaccine treatment is employed in the acute stage, these cases are cured before they become chronic. One characteristic feature of the vaccine treatment in sub-acute and chronic infections of the respiratory tract is the marked general improvement that is noticed before the local infection shows much change.

CATARRHALIS COMBINED VACCINE and INFLUENZA COMBINED VACCINE have proved most effective in the treatment of CORYZA, INFLUENZA, and other CATARRHAL CONDITIONS of the nose, throat and respiratory tract, as well as for immunization against these conditions. These vaccines are particularly useful in the Spring and Fall for immunizing persons who are subject to repeated colds.

DOSAGE: For prophylaxis, an initial dose of 150 million of CATARRHALIS COMBINED VACCINE or INFLUENZA COMBINED VACCINE should be followed in 3 days by an injection of 300 million; and the dose should be doubled at 3-day intervals thereafter until a total of 3 or 4 doses have been given.

In the treatment of acute affections, the initial dose of 150 million should be increased to 300 million on the second day; and the amount may then be increased

every 3 to 5 days according to indications until all symptoms of the disease have disappeared. If marked local or constitutional reaction follows, the subsequent dose should not be increased.

In the treatment of sub-acute and chronic catarrhal conditions, an initial dose of 150 million should be followed in 3 days by an injection of 300 million and the dose may be increased at 3- to 5-day intervals thereafter until the condition has been controlled.

QUANTITY IN CONTAINER: Catarrhalis Combined Vaccine (Mixed) is supplied in four dilutions:

No. 1 contains	25 million Mic. Catarrhalis. 25 million B. Friedlander. 25 million Pneumococci. 25 million Streptococci. 50 million Staphylococci (albus and aureus).
No. 2 contains	50 million Mic. Catarrhalis. 50 million B. Friedlander. 50 million Pneumococci. 50 million Streptococci. 100 million Staphylococci (albus and aureus).
No. 3 contains	100 million Mic. Catarrhalis. 100 million B. Friedlander. 100 million Pneumococci. 100 million Streptococci. 200 million Staphylococci (albus and aureus).
No. 4 contains	200 million Mic. Catarrhalis. 200 million B. Friedander. 200 million Pneumococci. 200 million Streptococci. 400 million Staphylococci (albus and aureus).

Influenza Combined Vaccine (Mixed) is supplied in four dilutions:

No. 1 contains	25 million B. Influenzae. 25 million Mic. Catarrhalis. 25 million B. Friedlander. 25 million Pneumococci. 25 million Streptococci. 50 million Staphylococci (albus and aureus).
No. 2 contains	50 million B. Influenzae. 50 million Mic. Catarrhalis. 50 million B. Friedlander. 50 million Pneumococci. 50 million Streptococci. 100 million Staphylococci (albus and aureus).
No. 3 contains	100 million B. Influenzae. 100 million Mic. Catarrhalis. 100 million B. Friedlander. 100 million Pneumococci. 100 million Streptococci. 200 million Staphylococci (albus and aureus).
No. 4 contains	200 million B. Influenzae. 200 million Mic. Catarrhalis. 200 million B. Friedlander. 200 million Pneumococci. 200 million Streptococci. 400 million Staphylococci (albus and aureus).

PREPARATION: These vaccines are prepared from cultures of the various organisms mentioned above after the manner described on page 12.

CONTAINERS: See page 70.

PACKAGES: For style of packages, see price-list.

Diphtheria

The rational treatment of Diphtheria has now been universally accepted by the medical profession to be the Antitoxic Serum treatment. Thousands of lives have been saved by the use of DIPHTHERIA ANTITOXIN, and many more cases of diphtheria could be saved by the early employment of large doses of antitoxin.

DOSAGE: For Immunization: Where children or adults have been exposed to diphtheria, they may be protected from the disease by the administration of 1,000 antitoxin units. The protection is absolute for ten days and usually lasts from three to four weeks. The injection should be repeated if danger of infection persists longer than two weeks.

For Curative Treatment: The dosage will depend entirely upon the apparent severity of the disease and the time that has elapsed since the onset of infection. In mild cases, if treatment is given early, 3,000 to 5,000 units may be sufficient; if treatment is delayed until the second day, or if the progress of the infection has been rapid, 7,500 or 10,000 units should be administered. In severe cases, in which the progress of the disease has been rapid and the infection involves a large area, and in all cases of nasal or laryngeal diphtheria, the dosage should be from 10,000 to 50,000 units.

In summing up the subject of dosage in the Cutter Lecture on Preventive Medicine, delivered at the Harvard Medical School, March 13, 1912, Dr. William H.

Park, Director of the Research Laboratories of the New York City Department of Health, says: "From all the observations, one is impressed with the belief that amounts of antitoxin beyond 25,000 units in a child, 50,000 units in an adult are absolutely unnecessary and useless; and that an initial dose of 10,000 in a child and 20,000 in an adult is probably sufficient for the whole course of the disease."

METHOD OF ADMINISTRATION: For Immunization: Diphtheria Antitoxin should be given subcutaneously at any point where there is sufficient subcutaneous tissue. For curative use, the subcutaneous method of administration may be used; but more rapid absorption is obtained by intra-muscular injection—preferably in the gluteal region. In severe or malignant cases, the antitoxin should be carefully warmed—not exceeding 98.6° F.—and very slowly administered intravenously.

At the point of injection, the skin should be painted with iodin, or cleansed with soap and water and rubbed with alcohol. Any air contained in the syringe should be expelled before injecting the antitoxin. After the operation, the site of injection may be protected with a sterile gauze dressing, or may be coated with collodion.

The earlier in the disease that the antitoxin is administered, the smaller the quantity of antitoxin that will be required to effect a cure. In case the desired dosage is not available, treatment should not be delayed; but injection of whatever antitoxin is obtainable should be

given at once. The favorable results following antitoxin treatment are in all probability due to the effects of the first injection, unless that injection was insufficient to neutralize the free toxin within the patient's body at that time; and second injections should not be required unless the necessary dosage at the first injection has been under-estimated. Therefore, it is far better, if 50,000 units are intended to be used in a given case, for the entire amount to be administered at one dose and as soon as possible after diagnosis has been made. The failure of diphtheria antitoxin to effect a cure can usually be attributed to delay in its use, or to its use in insufficient dosage.

QUANTITY IN CONTAINER: Lederle's DIPHTHERIA ANTITOXIN (Refined and Concentrated) is supplied in the following strengths: 500, 1,000, 2,000, 3,000, 4,000, 5,000, 7,500, and 10,000 units.

PREPARATION: In 1905, the Research Laboratories of the Department of Health of New York City perfected a practical method for separating diphtheria antitoxin in a refined and concentrated form from the blood serum of an immunized horse. In the following year, the Lederle Antitoxin Laboratories introduced to the medical profession the refined and concentrated diphtheria antitoxin product, prepared as directed by Robert B. Gibson, the originator of the method. By this process, those proteins which are insoluble in a half-saturated solution of ammonium sulphate and soluble in a

saturated solution of sodium chloride are retained; all other protein bodies are removed. Those proteins which are eliminated do not contain antitoxin and are undesirable in the antitoxin solution.

Later, it was demonstrated that, if the proteins retained by the above process were heated for several hours at 57° C., the solubility of certain inert protein matter contained therein was so changed that it was insoluble in a saturated sodium chloride solution, while the antitoxic protein remained soluble; thus permitting a further elimination of useless material.

By a combination of the above methods, in connection with their own modification, the Lederle Antitoxin Laboratories are able to eliminate about 60% of the protein originally present in immune horse serum; with the result that LEDERLE'S Diphtheria Antitoxin is today the most concentrated antitoxin ever offered to the medical profession—the low content of protein and salt insure rapid absorption and non-irritation. The final adjustment of the solution of refined and concentrated antitoxin is a most important feature. In the Lederle Antitoxin Laboratories, the solution is analyzed and carefully adjusted so that its reaction is very faintly alkaline to litmus: its content of protein does not exceed 18%; and the amount of inorganic salt is about 1.5%. To the finished solution, 0.35% trikresol is added as a preservative.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Erysipelas, Septicemia, Puerperal Sepsis, etc.

The causative factor of Erysipelas is now generally accepted to be some strain of the streptococcus; the staphylococcus, when present, playing a secondary role. In treating streptococcus infections with vaccines, it is important to employ a polyvalent vaccine because of the wide diversity of streptococcus strains. Lederle's STREPTOCOCCUS VACCINE is prepared from strains obtained from many different sources of infection; including scarlet fever, erysipelas, puerperal sepsis, etc. The results obtained from the use of STREPTOCOCCUS VACCINE and STAPHYLOCOCCUS-STREP VACCINE in the treatment of erysipelas have been very gratifying. COMBINED BACTERIAL VACCINE (Van Cott) is used especially in cellulitis and septicemia with good results. The streptococcus is also a complicating and causative factor in puerperal fever, rheumatism, septic sore throat, infected wounds, etc.

In fulminating cases, exhibiting extreme intoxication with lowered vitality of the patient, ANTISTREPTOCOCCUS SERUM given intravenously or subcutaneously will induce more rapid and favorable results than vaccine therapy. In order that best results may be obtained, however, it is essential that the serum be given early in the disease and in sufficiently large doses.

DOSAGE: The initial dose of STREPTOCOCCUS VACCINE is 10 million to 30 million. In erysipelas, 20 million seems to be a good, average adult dose; one-half of that amount being administered to children. The injections may be given every second or third day but if no improvement follows after 24 hours, another dose should then be given.

In puerperal sepsis, as well as in articular rheumatism, initial doses of 30 million of STREPTOCOCCUS VACCINE are usually employed; increasing the dose to 60 million or 100 million, if necessary. If no improvement is observed in 24 hours, the dose should be repeated.

The inital dose of STAPHYLOCOCCUS-STREP VACCINE varies from 75 to 125 million, subsequent doses being increased at 3 or 4 day intervals according to clinical manifestations.

The initial dose of COMBINED BACTERIAL VACCINE (Van Cott) is usually 0.5 c.c. (375 million of the combined organisms). This dose may be repeated at 3-day intervals according to clinical symptoms.

In general, the dosage of ANTISTREPTOCOCCUS SERUM—as laid down by the foreign investigators—should be for adults 150 c.c. to 200 c.c., followed in 24 to 48 hours by one-half this dose. The method of treatment employed and recommended by the Research Laboratory of the New York City Department of Health is to inject 200 c.c. of ANTISTREPTOCOCCUS

SERUM for the initial dose in adults: 100 c.c. being given in each side of the anterior abdominal wall. This dose is followed in 12 to 24 hours by one of 100 c.c. Further injections may be indicated, depending upon the character of the case, the extent of the toxemia, the result obtained, etc. For infants, the initial dose should be 50 to 100 c.c.

METHOD OF ADMINISTRATION: The method of administration of Antistreptococcus Serum will be found on pages 76-79.

QUANTITY IN CONTAINER: Streptococcus Vaccine is supplied in dilutions of 50 million, 100 million, 200 million, and 400 million.

Staphylococcus-Strep Vaccine is supplied in four dilutions. See page 30.

Combined Bacterial Vaccine (Van Cott formula) is supplied in one dilution:

50 million Streptococci.
100 million Pneumococci.
100 million B. coli communis.
500 million Staphylococci (albus, aureus, and citreus).

Antistreptococcus Serum is supplied in two strengths: 10 c.c. and 50 c.c.

PREPARATION: See pages 12 and 21.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Genito-Urinary Infections

The colon bacillus is the direct or complicating cause of numerous infections of the genito-urinary tract, including pyelitis, rectal abscess, ischio-rectal abscess, fistula in ano, sinuses, etc. COLON VACCINE is employed alone or in combination with other vaccines in the treatment of these infections.

DOSAGE: The initial dose of COLON VACCINE varies from 5 million to 50 million. A small initial dose is advised, after which the amount may be rapidly increased. At first, the injections may be given every 3 to 4 days; but later in the disease, intervals of 10 days are recommended.

QUANTITY IN CONTAINER: Colon Vaccine is supplied in dilutions of 50 million, 100 million, 200 million, and 400 million.

PREPARATION: See page 12.

CONTAINERS: See page 70.

PACKAGES: For style of packages, see price-list.

Gonorrhea and Gonorrheal Infections

The increasing appreciation of the serious nature of gonorrheal infections has tended to emphasize the necessity for bringing about the earliest possible eradication of the gonococcus. It is well known by all physicians that antiseptic solutions cannot reach the pathogenic or-

ganisms which have burrowed deeply into the mucous membrane; and it should be borne in mind that many of the most serious conditions result from the entrance of gonococci into the general circulation. The chief pathological conditions due to the gonococcus are: URETHRITIS, PROSTATITIS, EPIDIDYMITIS, VESICULITIS, ORCHITIS, VAGINITIS, ENDOMETRITIS, SALPINGITIS, ARTHRITIS, CONJUNCTIVITIS, CYSTITIS, ENDOCARDITIS. Treatment of these affections with GONOCOCCUS VACCINE has given brilliant results; the deep-seated infections responding more readily to the vaccine treatment. Gonorrhea is essentially a surface infection with a tendency to extend to deep-seated structures. The value of a vaccine consists in its specific influence in increasing the phagocyctic power of the blood, thus hastening the establishment of immunity; and naturally it will act more promptly where the infection is of such a nature that the blood comes thoroughly in contact with the organisms. The antibodies formed in response to the vaccine treatment circulate through the body fluids and the gonoccocci are destroyed; thus inducing a cure of the original infection and preventing the complications which otherwise would result when the gonococci gained entrance to the blood stream. The estimation of the value of GONOCOCCUS VACCINE depends largely on the viewpoint of the individual user and the kind of cases in which the vaccine is used. If, with a few inoculations of Gonococcus Vaccines, it is expected to effect a cure of acute or chronic

gonorrhea, in which other accompanying infective organisms are ignored, disappointment must inevitably follow.

GONOCOCCUS VACCINE is of value chiefly in the treatment of gonorrheal arthritis; vulvovaginitis of children; gonorrheal ophthalmia; salpingitis; and, to a variable degree, in acute urethritis. GONOCOCCUS COMBINED VACCINE is indicated in subacute gonorrhea; chronic posterior urethritis (gleet); and conditions due to mixed infection. Both of these vaccines are used in acute gonorrheal urethritis, but the results so far reported are variable; some clinicians reporting excellent results, and others, negative results. The deep-seated infections respond more readily to the treatment, and some brilliant results are reported in these cases.

In the treatment of chronic complications following the acute stage of gonorrhea—(1) those which occur as a result of direct extension of the primary infection into organs such as the prostate, bladder, epididymis, testicle, and Fallopian tubes; and (2) those due to the entrance of gonococci into the circulation, either directly or through the lymphatics, including arthritis, meningitis, pleuritis, endocarditis, and iritis—ANTIGONOCOCCUS SERUM is especially efficient.

DOSAGE: The inital dose of GONOCOCCUS VACCINE varies from 5 million to 15 million in the acute infections, and from 25 million to 50 million in chronic cases. The subsequent doses are usually doubled

if the symptoms warrant. Six to eight doses may be required in the acute cases at intervals of 3 to 5 days. In acute gonorrhea, local treatment should be employed in conjunction with the vaccine treatment; because the bacteria will continue to develop on the surface where phagocytosis cannot readily take place. Moreover, after the first few injections of the vaccine, the local discharge usually increases; but this increase is temporary, and should not be construed as indicating an aggravation of the condition.

In the treatment of gonorrhea, the question of mixed infections must be taken into consideration. In subacute and chronic gonorrhea, the staphylococcus is the principal and most constant accompanying organism. Many cases of chronic posterior urethritis, prostatitis, epididymitis, and gonorrheal rheumatism fail to respond to the administration of GONOCOCCUS VACCINE, because of the presence of staphylococci. Although the gonococcus is the specific cause of the disease, the staphylococcus aggravates and prolongs the condition. Unquestionably good results are being obtained with GONOCOCCUS COMBINED VACCINE (Mixed) in obstinate cases of chronic gonorrhea which previously had resisted all other treatment. Very often, too, an obstinate case of acute gonorrhea will yield to GONOCOCCUS COMBINED VACCINE (Mixed) when GONOCOCCUS VACCINE has given no result; because the staphylococcus is frequently found before the acute stage has subsided. As the staphylococcus is a most con-

stant complicating pathogenic organism in chronic gonorrhea, a practical method is to use the GONOCOCCUS COMBINED VACCINE (Mixed) as a routine treatment in these cases. The initial dose of the GONOCOCCUS COMBINED VACCINE (Mixed) will vary from 175 million to 500 million, gradually increased to 4,000 million or even 12,000 million; the injections being given every 3 to 7 days.

It is recommended that 10 c.c. of ANTIGONOCOCCUS SERUM be given as the minimum dose, which may be repeated as indicated by the clinical symptoms. In those conditions where the gonococci have gained entrance to the circulation and a profound toxemia exists, 50 or 100 c.c. may be required at one time. Moreover, as a general principal of serum therapy, in cases where the infection is severe, the administration at one time of a large quantity of serum produces far more satisfactory results than the repeated injections of small doses.

Recent reports from the Research Laboratory of the New York City Department of Health, in connection with the use of antibacterial serum, show that, in order to obtain the best results, it is necessary to use large doses—as much as 100 to 200 c.c. being administered at one time.

In cases treated with ANTIGONOCOCCUS SERUM, other measures known to be of value in the treatment of the condition may be employed without impairing the effect of the serum treatment.

METHOD OF ADMINISTRATION: Antigonococcus Serum is administered subcutaneously by using the Lederle Syringe. See top of page 15.

QUANTITY IN CONTAINER: Gonococcus vaccines include Gonococcus Vaccine and Gonococcus Combined Vaccine (Mixed). Gonococcus Vaccine is supplied in dilutions of 50 million, 100 million, 200 million, 400 million, and (in syringes only) 1,200 million. Gonococcus Combined Vaccine (Mixed) is supplied in 5 dilutions; the No. 5 being marketed in syringes only.

No. 1 contains	75 million	Gonococci.
	50 million	B. coli communis.
	75 million	Streptococci.
	300 million	Staphylococci (albus, aureus, and citreus mixed).
No. 2 contains	150 million	Gonococci.
	100 million	B. coli communis.
	150 million	Streptococci.
	600 million	Staphylococci (albus, aureus, and citreus mixed).
No. 3 contains	300 million	Gonococci.
	200 million	B. coli communis.
	300 million	Streptococci.
	1200 million	Staphylococci (albus, aureus, and citreus mixed).
No. 4 contains	600 million	Gonococci.
	400 million	B. coli communis.
	600 million	Streptococci.
	2400 million	Staphylococci (albus, aureus, and citreus mixed).
No. 5 contains	1200 million	Gonococci.
	800 million	B. coli communis.
	1200 million	Streptococci.
	4800 million	Staphylococci (albus, aureus, and citreus mixed).

Antigonococcus Serum is supplied in one strength: 10 c.c.

PREPARATION: See pages 12 and 21.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Hemophilia

Recently NORMAL HORSE SERUM has been extensively used with marked success in the treatment of HEMOPHILIA; also for other forms of hemorrhage—epistaxis, metrorrhagia, hemorrhage from wounds and fractures—and, in connection with surgical operations, to prevent post-operative hemorrhage.

HEMOPHILIA is a hemorrhagic diathesis or tendency to profuse or uncontrollable hemorrhage, occurring spontaneously or after some slight injury. Clinical evidence shows that the injection of NORMAL HORSE SERUM in hemophilic patients is followed by normal coagulability of the blood; and further, that this serum produces far better results than do gelatine, calcium, ergot, etc. In HEMOPHILIA NEONATORUM and hemorrhage from the umbilical cord, the use of NORMAL HORSE SERUM has given very gratifying results.

DOSAGE: Subcutaneously, 20 to 30 c.c. of NORMAL HORSE SERUM constitute the average adult dose; while for intravenous use, 10 to 20 c.c. will suffice —the injections being repeated if necessary at intervals of 2 days. In children, one-half of these doses are given.

In hemophilia, 10 to 30 c.c. is the usual dosage, repeated as necessary. In hemophilia neonatorum, and hemorrhage from the umbilical cord, 10 c.c. repeated three times daily or even every 2 hours should be administered.

As a preventive for post-operative hemorrhage, 20 c.c. of the serum is usually administered subcutaneously on the day before the operation.

QUANTITY IN CONTAINER: Normal Horse Serum is supplied in two strengths: 10 c.c. and 100 c.c.

PREPARATION: The same careful attention to details is observed by the Lederle Antitoxin Laboratories in the selection of healthy, vigorous animals, and in the preparation of Normal Horse Serum, as is carried out in the production of Lederle's refined and concentrated diphtheria antitoxin. The blood is withdrawn from the horses and allowed to clot. As soon as the serum separates, it is collected and 0.3% trikresol is added as a preservative. The serum is then allowed to remain in the ice-box for one week, after which it is passed through Berkefeld filters and placed in sterile containers. Before it leaves the laboratory, the serum is subjected to careful bacteriological tests in order to determine its sterility; and the absence of harmful in-

gredients is established by suitable inoculations into white mice and guinea pigs.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Meningitis

(Prophylaxis and Treatment)

As a curative agent, the value of ANTIMENINGOCOCCUS SERUM for Epidemic Cerebrospinal Meningitis is well known to every physician. But the prevention of this disease by immunization with MENINGOCOCCUS VACCINE has only recently been given serious consideration; although immunization by means of the subcutaneous injection of this vaccine during epidemics of the disease has been very effective, and the practice is now being widely employed. The serious nature of the disease should render prophylactic immunization a procedure to be adopted during every epidemic. The work of Flexner at the Rockefeller Institute has placed the serum treatment of Cerebrospinal Meningitis on a basis of approved value. The gravity method of administration of the serum is advocated by most clinicians; and the Lederle container has been devised for the express purpose of supplying a means for this method of administering the serum.

DOSAGE: MENINGOCOCCUS VACCINE is administered in three doses at intervals of 10 days; an initial dose of 500 million is followed by two successive

doses of 1,000 million each. The first immunizing dose sometimes produces headache, malaise, slight fever, and tenderness and redness about the site of the inoculation; but these symptoms pass off at the end of 24 to 48 hours.

The quantity of ANTIMENINGOCOCCUS SERUM introduced should be slightly less than the amount of fluid withdrawn. The dose is usually 5 to 15 c.c. in infants and children, and 30 c.c. or more in adults. The injections of the serum are to be repeated at intervals of 24 hours, and each injection is to be preceded by withdrawal of cerebrospinal fluid. Usually four to six injections of 5 to 15 c.c. each, at intervals of 24 hours, are required for infants and children; and a like number of injections of 30 c.c. each, at the same intervals, are necessary for adults; but as many as 15 or more doses may have to be given. If relapse occurs, repeat the doses at 24-hour intervals.

METHOD OF ADMINISTRATION: The method of administration of Antimeningococcus Serum will be found on pages 80-84.

QUANTITY IN CONTAINER: Meningococcus Vaccine is supplied in dilutions of 500 million and 1,000 million.

Antimeningococcus Serum is supplied in one strength: 15 c.c.

PREPARATION: See pages 12 and 21.

CONTAINERS: See page 70.

PACKAGES: For style of packages, see price-list.

Otitis Media

Acute Otitis Media is not only a very painful disorder, but it often leads to deafness; and, not infrequently, the infection extends into the mastoid cells resulting in mastoiditis. The importance of bringing this infective process rapidly under control with vaccine treatment can be readily appreciated. The important pathogenic organisms usually found in acute Otitis Media are the streptococcus, staphylococcus and, at times, the pneumococcus. In treating this condition, PNEUMOCOCCUS COMBINED VACCINE is being extensively employed by many otologists. If the vaccine is given early, the ear drum may often be saved; but if there is much bulging of the drum, it should be lanced. Where the ear drum is punctured, it will be found that the discharge will dry up in much less time if STAPHYLOCOCCUS-STREP VACCINE or PNEUMOCOCCUS COMBINED VACCINE is used.

Bacterial examination of the pus in the early stages of Suppurative Otitis Media show that in a large majority of cases the streptococcus is the primary infecting organism. After a rupture of the ear drum, contamination soon takes place and staphylococci are found. In treating these cases, therefore, STAPHYLOCOCCUS-STREP VACCINE will be found to be a valuable means of hastening recovery.

DOSAGE: The initial dose of PNEUMOCOCCUS COMBINED VACCINE and STAPHYLOCOCCUS-

STREP VACCINE varies from 75 to 125 million, subsequent doses being increased at 3- or 4-day intervals, according to clinical manifestations.

QUANTITY IN CONTAINERS: See pages 30 and 55.

PREPARATION: See page 12.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Pneumonia

LOBAR PNEUMONIA is still one of the most fatal diseases. The pneumococcus is recognized as the pathogenic factor in this disease, although the streptococcus is also frequently found and in such cases is no doubt a complicating factor. In this highly fatal disease, the early use of PNEUMOCOCCUS VACCINES is strongly indicated. Severe forms of pneumonia, which show a pronounced toxemia, should be treated with ANTIPNEUMOCOCCUS SERUM, thereby placing antibodies in the blood stream at once. ANTIPNEUMOCOCCUS SERUM is especially useful in cases of lobar pneumonia. It exerts an abortive influence, for the temperature falls permanently and by lysis instead of by crisis; and there is a change in the physical signs, which indicate that the consolidated area is undergoing resolution. The most marked value of this serum is obtained when it is administered early and in large doses!

No. 3 contains	200 million Pneumococci. 100 million Streptococci. 200 million Staphylococci (albus, aureus, and citreus mixed).
No. 4 contains	400 million Pneumococci. 200 million Streptococci. 400 million Staphylococci (albus, aureus, and citreus mixed).
No. 5 contains	800 million Pneumococci. 400 million Streptococci. 800 Million Staphylococci (albus, aureus, and citreus mixed).

Antipneumococcus Serum is supplied in two strengths: 10 c.c. and 50 c.c.

PREPARATION: See pages 12 and 21.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Pyorrhea Alveolaris

Local infections caused by the streptococcus and pneumococcus, such as pyorrhea alveolaris, are being effectively treated with STREPTOCOCCUS COMBINED VACCINE and PNEUMOCOCCUS COMBINED VACCINE.

DOSAGE: See pages 54 and 57.

Rheumatism

The specific causative agent of acute articular rheumatism has not yet been definitely proven; but extensive

research by numerous investigators has demonstrated the presence of streptococci in the joint fluid, and clinicians are constantly reporting favorable results from the use of STREPTOCOCCUS COMBINED VACCINE in articular rheumatism. The subsidence of pain is the first symptom of relief, followed by lessened inflammation of the joints. A very important feature of the vaccine treatment of articular rheumatism is that it materially reduces the number of heart complications which so commonly follow this disease.

DOSAGE: The initial dose varies from 50 to 150 million, increased according to clinical symptoms.

Scarlet Fever

(Prophylaxis and Treatment)

The bacteriology of scarlet fever has been extensively studied for many years, but only during the past year has anything of a definite nature been published regarding the bacterial etiology of this disease. For some time, it has been recognized that the streptococcus is a complicating infective organism in many cases of scarlet fever. From the work of various investigators, it seems evident that the streptococcus is closely connected with scarlet fever infection. The exanthematous diseases have so far resisted all attempts to isolate their specific causative agent; scarlet fever is the only one in which progress has been made. In this disease, it has been shown that, whether or not it is the causative factor, much of the severity of the disease and practically all of

the sequelae are due to the streptococcus. A polyvalent bacterial vaccine composed of streptococci obtained from several cases of scarlet fever is being extensively employed for the prophylaxis as well as for the treatment of scarlet fever. The prophylactic use of STREPTOCOCCUS VACCINE in scarlet fever is receiving much attention, especially by Russian physicians, whose statistics appear to show a remarkable immunity to the disease in those who have received the protective vaccines. The results have been so satisfactory that SCARLET FEVER PROPHYLACTIC and SCARLET FEVER TREATMENT are rapidly coming into general use. In the treatment of scarlet fever, especially in severe cases, the use of ANTISTREPTOCOCCUS SERUM is giving favorable results.

DOSAGE: SCARLET FEVER PROPHYLACTIC (Streptococcus Vaccine) is administered in 3 doses at intervals of 7 days; the initial dose is 250 million; the second dose is 500 million; and the third dose is 1,000 million. Complete immunity against scarlet fever is established after the third inoculation; but the immunity is not fixed until 6 or 7 days after the third dose has been administered.

The initial adult dose of SCARLET FEVER TREATMENT is usually 30 to 50 million, while children receive about one-half of this amount. Subsequent doses may be increased—the amount being regulated by clinical observations.

For dosage of ANTISTREPTOCOCCUS SERUM, see page 40.

QUANTITY IN CONTAINER: Scarlet Fever Prophylactic (Streptococcus Vaccine from strains from scarlet fever cases) is supplied in dilutions of 250 million, 500 million, and 1,000 million.

Scarlet Fever Treatment (Streptococcus Vaccine from strains from scarlet fever cases) is supplied in dilutions of 50 million, 100 million, 200 million, and 400 million.

Antistreptococcus Serum is supplied in two strengths: 10 c.c. and 50 c.c.

PREPARATION: See pages 12 and 21.

CONTAINERS: See page 70.

PACKAGES: For styles of containers, see price-list.

Tetanus

Many traumatisms, such as blank cartridge wounds, nail punctures, machinery wounds, crushes, and other injuries into which dirt is carried into a deep wound are more or less liable, according to the region of the country, to be followed by tetanus. The danger is especially great when the dirt is ground into the injured tissues: street dust and garden-soil are particularly apt to contain tetanus organisms. In many localities the danger is much greater than in others; where tetanus is prevalent,

the horse manure is generally infected, as the tetanus bacilli grow in the intestines of this animal and the spores remain alive in the dirt for years. In cases where the wounds are extensive and it is impossible to thoroughly clean the wounds, it is advisable to give a second prophylactic injection of antitoxin at the end of ten days. TETANUS ANTITOXIN is used both as a prophylactic and therapeutic agent. TETANUS ANTITOXIN is almost an absolute specific against the development of tetanus, when given within 12 or 24 hours after the injury.

METHOD OF ADMINISTRATION: As a prophylactic, Tetanus Antitoxin is usually given subcutaneously at any point where there is sufficient subcutaneous tissue. By this method, the antitoxin is given out into the circulation slowly, and is not, therefore, eliminated rapidly; so that the immunity will persist for the maximum period. In cases where the wound has been neglected for several days, however, it is better to administer the antitoxin as near to the wound as possible, so as to flood the tissues in the immediate vicinity; and the injection should be deep, intra-muscular if possible, so as to permit its rapid absorption by the motor nerves. If any nerves are exposed in the wound, the antitoxin should be injected into them. It appears to be a well-ascertained fact that most of the antitoxin is eliminated from the system in about 8 or 10 days after the injection; hence, it is advisable to administer a second prophylactic dose at

the end of 8 or 10 days, in order to maintain the immunity induced by the first injection.

For curative use, four methods of administration of Tetanus Antitoxin are advocated: namely, subcutaneous, intravenous, intraspinal and intraneural.

1. Subcutaneous Injection. This is the method which has been usually employed, but the reports are not encouraging. If administered in this way, the antitoxin is absorbed by the lymphatics, transported to the veins, passes through the lungs and finally is distributed through the arterial system to all parts of the body. Only a very small dose ultimately reaches the motor nerves, through which the toxin is being carried to the spinal cord, while by far the greater part of the antitoxin is distributed to the viscera, where it can be of no possible use.

2. Tetanus Antitoxin administered only by the intravenous method is not very effective; the amount required by this route to produce any therapeutic effect is enormous, as is proved by the observation of various investigators.

3. Intraspinal Injection. Experimentally, treatment of tetanus by intraspinal injections of tetanus antitoxin has not been very encouraging, but much more satisfactory results have been obtained in actual practice.

4. Intraneural Injection. This method was first employed clinically by Kuester in 1902. As it is a well-ascertained fact that most and possibly all of the toxin reaches the spinal cord only by traveling up its nerves, it is

theoretically logical to inject the antitoxin into the nerves in order that, like the toxin, it may reach the spinal cord by the easiest route. That it will do this, when injected intraneurally, admits of no doubt, in view of the overwhelming experimental evidence on this point. Just how the antitoxin acts, and by which intraneural route it reaches the cord, has not been determined. The only possible methods for reaching all the nerves at once are (1) intravenous injections, and (2) intraspinal injections. In no case, therefore, should the surgeon depend on intraneural injections alone, and in no case should he omit either intraspinal injections or injections into the motor nerves leading from the site of inoculation, or intravenous injections. In the patients who have recovered after this form of treatment, no disability appears to have been caused.

Regardless of the method of administration, the most important thing in the treatment is to give the maximum quantity of antitoxin indicated as soon as possible, for delay, even of a few hours, may mean a fatal result. It is desirable for the entire amount of antitoxin to be administered at one time and as soon as possible after diagnosis has been made.

DOSAGE: For Immunization: The immunizing dose agreed upon by a committee of American Bacteriologists as sufficient to protect against the development of tetanus within the incubation period is 1,500 units of American standard. For Curative Treatment: If the

injections are given subcutaneously, 100,000 units will be required in the first 24 hours for the usual acute type of case in an adult, and although a smaller amount may be sufficient for a child or for an apparently mild case, one cannot be sure of that fact, and it is better to give too much than too little. If administered intravenously, probably 20,000 to 40,000 units should be administered at first and repeated after the lapse of 18 to 24 hours. If given intraspinally, from 3,000 to 10,000 units should be given according to the severity of the case, and this dose need not, as a rule, be repeated in less than 18 or 24 hours. If given intraneurally, injections of antitoxin should be made in as great amount as the nerve-sheaths will contain; for example, 1,500 units in the sciatic nerve and 750 units in the anterior crural or obturator nerves. If the injections are made slowly, practically all of this quantity can be introduced among the nerve fibers.

The most logical antitoxic treatment of tetanus is to administer the antitoxin intraspinally and intravenously in all cases; and intraneural injections should be made whenever possible.

QUANTITY IN CONTAINER: Refined and concentrated Tetanus Antitoxin is supplied by the Lederle Antitoxin Laboratories in the following strengths: 1,500, 3,000 and 5,000 units.

PREPARATION: In 1905, the Research Laboratories of the Department of Health of New York City perfected a practical method for separating diphtheria

antitoxin in a refined and concentrated form from the blood serum of an immunized horse. In 1907, the Lederle Antitoxin Laboratories introduced to the medical profession the refined and concentrated tetanus antitoxin product, prepared by the method outlined by Robert B. Gibson and employed in the preparation of Lederle's Diphtheria Antitoxin, as described on page 37.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Typhoid Fever

(Prophylaxis and Treatment)

TYPHOID VACCINE (PROPHYLACTIC) is now employed as an immunizing agent in all the important armies of the world. In the United States Army and Navy, all officers and enlisted men under 45 years of age are immunized against typhoid fever. Realizing the tremendous saving and the benefit derived from prophylactic immunization against typhoid fever, many corporations, where large numbers of men are employed, are now recommending typhoid inoculation to the employees.

In the treatment of typhoid fever, no single remedy has proven of such value as TYPHOID VACCINE. Very encouraging results are constantly being reported; the fever becomes milder and of shorter duration; fewer relapses occur; and complications are lessened.

PARATYPHOID FEVER, being very similar to typhoid, is frequently confused with it. Clinically, this disease resembles typhoid fever, but usually follows a mild course. By careful technique, many cases of fevers now classed as "undetermined" may possibly be found to be paratyphoid. TYPHOID COMBINED VACCINE is now coming into general use as an immunizing agent against paratyphoid fever, as well as against typhoid fever, inasmuch as this vaccine contains both the typhoid and paratyphoid bacilli.

DOSAGE: As an immunizing agent, TYPHOID VACCINE (PROPHYLACTIC) is administered in three doses at intervals of ten days; an initial dose of 500 million is followed by two successive doses of 1,000 million each. The first immunizing dose sometimes produces headache, malaise, slight fever, and tenderness and redness about the site of the inoculation; but these symptoms pass off at the end of 24 to 48 hours.

In the treatment of typhoid fever, very encouraging results are constantly being reported with TYPHOID VACCINE. At first, the therapeutic dose consisted of 25 million administered every second day; but lately, better results seem to be achieved by giving 300 million as the initial dose and increasing 100 million every second or third day until 1,000 million are given at a dose. The vaccine treatment ought to be given as soon as a diagnosis is made, and should be continued until the temperature becomes normal.

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TYPHOID COMBINED VACCINE (Mixed) is administered as an immunizing agent in three doses at intervals of ten days; an initial dose of 1,000 million is followed by two successive doses of 2,000 million each. The first immunizing dose sometimes produces headache, malaise, slight fever, and tenderness and redness about the site of the inoculation; but these symptoms pass off at the end of 24 to 48 hours.

QUANTITY IN CONTAINER: Typhoid Vaccines include Typhoid Vaccine (Prophylactic), Typhoid Vaccine and Typhoid Combined Vaccine (Mixed). Typhoid Vaccine (Prophylactic) is supplied in dilutions of 500 million and 1,000 million, for administration in three doses. Typhoid Vaccine is supplied in dilutions of 100 million, 250 million, 500 million, and 1,000 million.

Typhoid Combined Vaccine (Mixed) is supplied in two dilutions—1,000 million and 2,000 million killed bacteria—for adminstration in three doses.

Initial dose contains	500 million B. Typhosus. 250 million B. Paratyphosus "A" 250 million B. Paratyphosus "B"
Second dose contains	1000 million B. Typhosus. 500 million B. Paratyphosus "A" 500 million B. Paratyphosus "B"
Third dose contains	1000 million B. Typhosus. 500 million B. Paratyphosus "A" 500 million B. Paratyphosus "B"

PREPARATION: See page 12.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Whooping Cough
(Pertussis)

It has recently been demonstrated that the specific causative agent of whooping cough (pertussis) is the Bordet bacillus, discovered by Bordet and Gengou. Early in the course of the disease, this bacillus is present in large numbers, but later it is associated with the influenza bacillus, the pneumococcus and other micro-organisms—the presence of which favor the development of broncho-pneumonia, which so frequently causes a fatal termination of this widespread disease. While the reports of clinicians in regard to the use of PERTUSSIS VACCINE have not been numerous, nevertheless they have been invariably favorable and have proven conclusively the value of vaccine therapy in this disease. Moreover, the reports have always shown the absolute freedom from harmful effects, even in very young babies.

The reports so far received from clinicians who have used PERTUSSIS VACCINE in large numbers of cases of whooping cough show that this vaccine, when used as a prophylactic agent, will absolutely prevent the disease. The immunity is of uncertain duration, but probably lasts for at least 6 months. In the treatment of WHOOPING COUGH, the use of PERTUSSIS VACCINE has very materially shortened the course of the disease and lessened the severity of the paroxysms; many severe cases entirely subsiding under this form of treatment within 4 weeks after the institution of vaccine therapy. In the

late stages of the disease, PERTUSSIS COMBINED VACCINE is particularly valuable for the purpose of combating the complications, such as broncho-pneumonia.

Recent research work has demonstrated that the Bacillus influenzae and the Pneumococcus are almost constantly present with the Bordet bacillus in whooping cough; moreover, after the first week of the disease these organisms outgrow the Bordet bacillus and become the chief infecting agents.

DOSAGE: In using PERTUSSIS VACCINE for prophylaxis, three doses of 25 million, 50 million and 100 million are given at 7-day intervals. In the treatment of whooping cough, Pertussis Vaccine is employed in initial doses of 25 million, increased to 50 or 100 million. The vaccine is usually given every second day; but some clinicians now advise, especially in severe cases, that doses of 50 to 100 million be administered daily.

PERTUSSIS COMBINED VACCINE (Mixed) is employed for immunization in initial doses of 150 million, followed in 7 days by an injection of 300 million; and, one week later, by a dose of 600 million. In the treatment of whooping cough, an initial dose of 150 million is increased to 300 million, 600 million, or 1,200 million; the doses being given daily or every 2 or 3 days.

PERTUSSIS VACCINES diminish the severity and number of the paroxysms of whooping cough, and

shorten the course of the disease. No harmful effects have been noted—freedom from complications appears to be one of the favorable effects of the treatment. The place best adapted for administering the vaccines is in the interscapular region, where the child cannot easily scratch.

QUANTITY IN CONTAINER: Pertussis Vaccines include Pertussis Vaccine and Pertussis Combined Vaccine (Mixed). Pertussis Vaccine is supplied in dilutions of 25 million, 50 million, 100 million and 200 million. Pertussis Combined Vaccine (Mixed) is supplied in four dilutions:

No. 1 contains	25 million B. Pertussis (Bordet). 25 million B. Influenzae. 25 million Pneumococci. 25 million Streptococci. 50 million Staphylococci (albus and aureus).
No. 2 contains	50 million B. Pertussis (Bordet). 50 million B. Influenzae. 50 million Pneumococci. 50 million Streptococci. 100 million Staphylococci (albus and aureus).
No. 3 contains	100 million B. Pertussis (Bordet). 200 million B. Influenzae. 100 million Pneumococci. 100 million Streptococci. 200 million Staphylococci (albus and aureus).

No. 4 contains 200 million B. Pertussis (Bordet).
200 million B. Influenzae.
200 million Pneumococci.
200 million Streptococci.
400 million Staphylococci (albus and aureus).

PREPARATION: See page 12.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Containers

The products of the LEDERLE ANTITOXIN LABORATORIES are supplied in the following types of containers:

The Lederle Vial

THE LEDERLE VIAL: This vial has been designed to hold the various dilutions of Bacterial Vaccines

such as are ordinarily used in practice; the dilutions being indicated on the label which is so graduated that any desired portion of the contents of the vial may be used for a single dose. The vial is sealed with a hollow rubber stopper—the outer surface of which may be sterilized with cresol or lysol—which can be easily punctured with a hypodermic needle; thus avoiding the necessity of

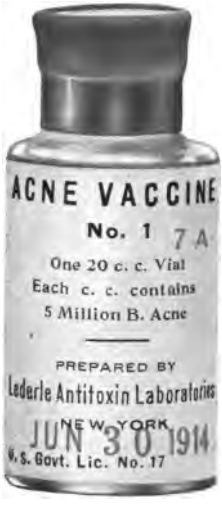
Partly withdraw piston from syringe.
Puncture the rubber stopper with hypodermic needle.
Push the piston forward, forcing the air in the syringe into the vial.

removing the stopper or breaking the glass, and permitting the contents to be withdrawn into a hypodermic syringe under aseptic conditions. The method of using the Lederle Vial is illustrated above and on next page.

Withdraw the piston holding the vial so that liquid covers point of needle.

THE 20 C.C. VIAL: This container was specially designed as a bulk package to contain sufficient Bacterial Vaccine for several doses; and is intended for use where the physician has conveniences for sterilizing his own graduated hypodermic syringe. The vial is sealed with a soft rubber stopper—the outer surface of which may be sterilized with cresol or some other suitable antiseptic —which can be easily punctured with a sterilized hypodermic needle and the desired amount of Bacterial Vaccine withdrawn into a syringe. This style of container

The 20 c.c. Vial



readily permits of any desired amount of the vaccine being administered and at the same time preserves the remainder of the contents for future use; for the puncture, made in the stopper by the needle, will close when the needle is withdrawn—thus sealing the vial hermetically.

THE LEDERLE SYRINGE: This syringe possesses the following advantages: It is (1) aseptic, (2)

convenient, (3) ready for instant use, (4) reliable and (5) it works as easy as an ordinary syringe. The Lederle Syringe container has been devised to furnish physicians

The Lederle Syringe

with a convenient instrument with which to administer antitoxins, serums and bacterial vaccines.

It consists of a glass barrel closed at one end by the piston which is constructed of rubber and asbestos, pro-

ducing a piston which has very little rubber surface in contact with the glass, thus preventing any appreciable adhesion and difficulty in starting the piston; the rubber flanges being sufficient only to prevent evaporation of the contents or absorption by the asbestos. The other end is closed by a specially molded stopper, which is perforated to receive the needle. The outer end of the stopper is sealed with a rubber membrane which can be

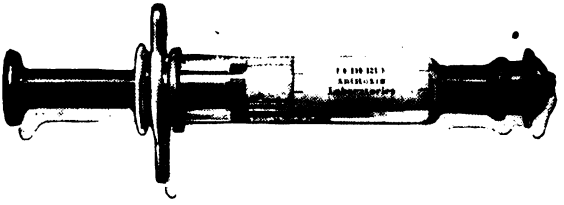


Figure 1 shows the syringe as the physician receives it.

easily removed by means of the attached flange. A sterilized hypodermic needle ready for use is provided in a sterile glass tube with each syringe; and the contents of the syringe is injected directly into the patient. The syringe when filled with a Bacterial Vaccine has a graduated scale on its barrel, thereby enabling the physician to inject any desired portion of the contents.

Figure 2 shows the needle wrapped and encased in a glass tube in which it has been sterilized.

Figure 3 shows the needle with the paper wrapping removed.

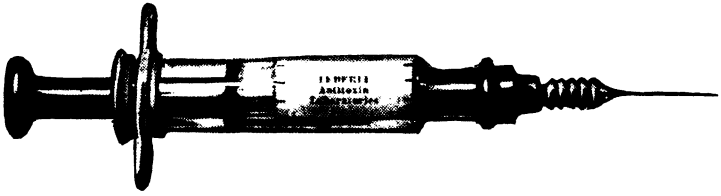
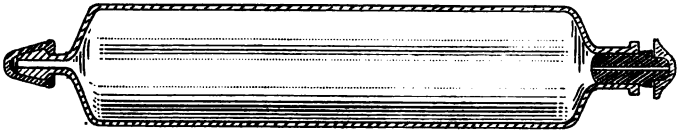


Figure 4 shows the syringe connected with the needle and ready for the operation.

THE 50 C.C. GLASS CYLINDER: The illustration on next page shows the complete outfit for administering Lederle's ANTISTREPTOCOCCUS SERUM, and Lederle's ANTIPNEUMOCOCCUS SERUM.

The 50 c.c. Cylinder



Cross section of Cylinder.

Cross Section of Needle and Connection.

DIRECTIONS FOR USING CYLINDER: Remove the flanged cap from large end of cylinder, thus exposing perforation in rubber stopper. Remove the wrapping from end of needle connection, and force the metal end through the perforation in the rubber stopper. Hold the cylinder vertically and remove rubber cap from small (upper) end of cylinder until serum comes out of needle; then replace the cap. Hold needle, with attached cylinder, in usual manner for making subcutaneous injection. After needle is inserted into the tissues up to its hub, remove cap from opposite end of cylinder and adjust rubber tubing with attached glass union, containing cotton filter, to exposed end of cylinder. Adjust rubber bulb to glass union and proceed to inject the serum. Compress the bulb repeatedly until sufficient pressure has been attained to cause a slow injection of the serum: as injection proceeds, further compression of the bulb will be required to maintain pressure sufficient to com-

plete the injection. (Do not use too great compression, as a slow injection of the serum is to be desired.) A fairly rapid flow of serum will take place without visibly lowering the surface of the liquid in the cylinder at a rapid rate.

As administration of the serum proceeds, hold the cylinder vertically, so that no air will be forced into the tissues. When all but a few drops of serum have been injected, remove rubber tubing from top of cylinder and withdraw needle.

METHOD OF ADMINISTRATION of Antipneumococcus Serum and Antistreptococcus Serum: These serums are generally administered subcutaneously. The injections are best made by inserting the needle deeply into the subcutaneous tissues of one side of the lower abdomen, where there is ample loose subcutaneous tissue. It is desirable to inject not more than 100 c.c. in one place; if a larger dose than this is given, the opposite side of the abdomen may be used. The swelling caused by this amount of serum is formidable, and the tension at times is very great; but after the first 2 or 3 c.c. have been injected, there is no pain and very little discomfort—the serum being rapidly absorbed. At the point of injection, the skin should be painted with iodin, or cleansed with soap and water and followed by alcohol. The serum should be injected very slowly and deeply into the subcutaneous tissues; and, upon withdrawal of the needle, the site of injection may be protected with a sterile gauze dressing, or may be coated with collodion.

THE 15 C.C. GLASS CYLINDER: The following photograph illustrates the complete outfit for administration of Lederle's ANTIMENINGOCOCCUS SERUM by the gravity method.

The 15 c.c. Cylinder

DIRECTIONS FOR ADMINISTERING ANTIMENINGOCOCCUS SERUM by the gravity method:

The serum is administered intraspinally; the subcutaneous or intravenous routes being practically worthless. The technique includes that required for performing a lumbar puncture, inasmuch as the serum must be introduced into the spinal canal after the withdrawal of cerebrospinal fluid.

The patient is placed on the side, with head bent forward and knees drawn up. The skin, in the lumbar region of the back, is painted with iodin, or washed with soap and water and followed by alcohol and ether. The operator, whose hands have been sterilized, takes the sterilized needle with its contained stylet in his right hand and introduces the needle through the intervertebral disc between the third and fourth lumbar vertebrae, and a little to one side of the median line; the thumb of the left hand being placed between the spinous processes as a guide. The point for inserting the needle may be conveniently located by placing the index and third fingers of the left hand on the highest points of the iliac crests. The middle finger will then rest on the third lumbar spine, and the point of election is midway between this spine and the one immediately below it. The needle should be cautiously pushed forward until the slight resistance of the dura is felt; this occurs at a depth of about two centimeters (¾ inch) in infants, and at 4

to 6 centimeters (1½ to 2 inches) in adults. If bony resistance is encountered, withdraw the needle slightly and change the angle of insertion. As soon as the dura has been punctured, the stylet should be withdrawn, and cerebrospinal fluid will begin to flow from the needle. The fluid is usually cloudy or turbid, and escapes slowly; if there is no flow, or if the flow ceases too soon, the needle may be rotated or its lumen freed by the introduction of the stylet, or the needle may be introduced a trifle further. The flow may be increased by placing the patient in a sitting posture. The fluid should be allowed to flow from the needle into a sterilized test tube, and should be examined bacteriologically to determine the presence of meningococci. However, the serum should be injected immediately without waiting for bacteriologic examination; but a second injection of serum is not to be given until examination of the cerebrospinal fluid shows the presence of the meningococcus. In infants and young children, about 15 to 20 c.c. of fluid may be withdrawn; and in adults, 40 to 60 c.c.; the fluid being allowed to flow until the cerebrospinal fluid pressure falls to normal; one drop from the needle every 3 to 5 seconds being about normal.

After the fluid has been withdrawn, the glass cylinder is attached to the needle, which is left in position; and the serum, having been gently warmed to body temperature, is allowed to flow into the spinal cavity by gravity. (Care must be exercised not to heat the serum above 98.6° Fahrenheit; otherwise it may coagulate!)

The adjustment of glass cylinder to needle is effected in the following manner:

Withdraw the soft cotton cord from the rubber tubing (the cord prevents collapse of tubing while in the package); remove one of the rubber caps from the glass cylinder, and slip rubber tubing over the exposed end of cylinder. Hold the cylinder vertically and remove rubber cap from upper end of cylinder until serum escapes from metal tip of rubber tubing (thus expelling all air from tubing); then replace the cap and firmly insert the metal tip of rubber tubing into hub of needle. Now remove the rubber cap from upper end of glass cylinder, and adjust the rubber portion of rubber-and-glass union to exposed end of the glass cylinder. (The cotton filter, in glass portion of union, prevents any foreign matter from gaining access to, and contaminating the serum.) It will require from 10 to 25 minutes for the serum to be introduced into the spinal canal. The flow may be increased or decreased by raising or lowering the glass cylinder. The physician is enabled to observe, by means of the short glass tubing near metal tip of rubber tubing, the instant that all of the serum has been introduced; and thus air can be prevented from being forced into the spinal canal.

If 30 c.c. or more of fluid have been withdrawn, the entire contents of the glass cylinder is introduced; after which the cylinder is detached from the needle, which is not withdrawn, and another cylinder attached and its contents introduced in a similar manner.

When the desired amount of serum has been introduced, the needle with the attached glass cylinder is rapidly withdrawn, and the puncture wound is sealed with collodion. The patient should be placed in a recumbent posture and, if there is delirium or severe headache, the patient's head should be lowered.

Symptoms of shock or collapse, during the injection of the serum, are best treated by raising the head of the patient and immediately removing fluid from the spinal canal. If necessary, use artificial respiration and administer stimulants hypodermically.

If it is desired to use the pressure method for introducing the serum, an atomizer bulb may be attached to the glass end of rubber-and-glass union and the serum injected very slowly without pressure—at the rate of about 2 c.c. per minute.

RABIES
and
SMALLPOX

Vaccines for their
Prophylaxis

Rabies

HISTORICAL: Rabies is a rapidly fatal, highly acute, specific disease to which all warm-blooded animals are susceptible. Of the domestic animals, dogs are most frequently infected and are usually responsible for the transmission of the disease to human beings. Rabies has been known for more than 2,300 years; the earliest reference to the disease is that of Aristotle in the fourth century, B. C.

During the year 1912 there were more than 4,000 cases of rabies in this country which, in this unenviable respect, leads all the nations of the world—with the exception of Italy. Australia has never had the disease, but this is due to the efficiency of its quarantine against animals. The disease can be prevented by enforced muzzling of dogs, and there has not been a single case in England since the muzzling law went into effect in 1902.

NATURE OF THE DISEASE: Rabies is transmitted to human beings through inoculation with virus from infected animals—usually dogs. The saliva of the animal is the infecting medium which conveys the poison. When infection occurs, following the bite of a rabid animal, no symptoms—apart from the wound—are noted for a variable length of time, depending upon the severity of the bite, location of the wound, etc. An infected wound on the head is usually followed by symptoms of the disease within a shorter period than a wound on the

hand or foot. The period of time that elapses between the biting by the animal and the development of symptoms in the individual is known as the period of incubation. This varies from ten days to six months or longer —the majority of cases occur before the end of the third month—the average time being about seventy-two days.

SYMPTOMS IN THE DOG: Rabies presents at least two clinical types: these are the excited, and the paralytic. It is important that the early symptoms of rabies in the dog be recognized; for the bite of a dog may communicate the disease three or five days prior to the development of symptoms in the dog. At this stage, the animal may be playful and affectionate to an unusual degree; he desires to be recognized and petted. Later, there is a marked change in the voice to a hoarse howl, followed by an unequal series of barks, lower in pitch than is normal. The rabid dog becomes restless, lying down and getting up again repeatedly. He is easily startled, growls and barks on slight provocation.

In the excited type, the dog may suddenly leave home, wandering off for many miles, to return in a day or two, emaciated, wounded, and utterly changed. During the period of running mad, he may have bitten many persons and animals. He does not fight other dogs, but bites them and passes on. The dog looks sick, and takes no interest in his surroundings. It is the rule that dogs in this condition have no appetite for their accustomed food and frequently swallow indigestible objects. Swal-

lowing is difficult and, later in the disease, impossible. Convulsions now appear, and the dog may die in one. More frequently a paralytic stage supervenes: the animal drags himself to a secluded spot; the hind legs become paralyzed first, giving the impression that the spine is injured. Saliva drools from the mouth and the dog becomes much emaciated.

The paralytic form is quite frequent among dogs and offers peculiar danger to man. These are the cases where the owner or bystander endeavors to remove an imaginary bone from the throat and becomes bitten. Spasms of deglutition and paralysis of the throat muscles strongly suggest an obstruction in the throat. It is a mistake to suppose that rabid dogs have any fear of water. They are intensely thirsty and desire to drink, but when the paralytic condition affects the throat muscles they are unable to swallow. They are so far from having a fear of water that they sometimes swim rivers while in the excited stage, as observed in ancient and modern times. The term hydrophobia—meaning fear of water—is a misnomer, and should be discarded.

CARE OF WOUND: All wounds should be cauterized as soon as possible—it is never too late to derive some benefit from cauterizing. Thorough cleansing with antiseptic solutions should be followed by the application of undiluted formalin or nitric acid; and an aseptic dressing may then be applied. Whenever there is any reason to suspect that the animal—which was responsible for the wound—may have had rabies, then, in addition to

the cauterization and dressing of the wound, arrangements should be made at once for the administration of Rabies Vaccine in the form of preventive treatment prepared after the method of Pasteur.

CARE OF PATIENT: The bowels should be kept freely open during the course of treatment, and the drinking of tea, coffee and alcoholic beverages allowed but sparingly. While taking the antirabic treatment, patients are ordinarily able to attend to their work. Exposure to cold, especially excessive bathing, should be avoided during the course of treatment. Some local soreness, together with erythema about the site of the injection, may occur. If these signs of reaction are marked, the application of a wet dressing of aluminum acetate solution will be found useful. Slight malaise may also be felt. The laboratories should be notified by telegraph of any unusual symptoms.

HOW TO SECURE TREATMENT: Requests for treatment should be telegraphed to Lederle Antitoxin Laboratories, Pearl River, New York; stating age of patient, date, location, and severity of bite, and full name and address of physician to whom treatment is to be sent. Freshly prepared Rabies Vaccine is kept in constant readiness to immediately fill all orders. The Lederle Antitoxin Laboratories are prepared to promptly furnish to the medical profession the complete course of antirabic treatment, ready for use, with full equipment. Lederle's Rabies Vaccine is supplied in a package be-

lieved to be ideal, so that no time need be wasted before beginning treatment. Instructions are furnished with the treatment, and the technique is simple and easily within the scope of every practising physician.

Until recently it has been necessary to go to special institutions maintained for the purpose of giving antirabic treatment. This has practically made it impossible for the physician to avail himself of this treatment for his patients. During the last few years, however, it has been clearly demonstrated that it is possible to supply this treatment in such form as to admit of its use by any physician, irrespective of previous experience in administering the treatment, and without removing the patient from his surroundings. The ability of the family physician to administer this treatment in the patient's own home is heartily welcomed by the patient.

INDICATIONS: Rabies Vaccine is used for the preventive treatment of rabies during the incubation period. After symptoms of the disease are fully developed, antirabic treatment is of absolutely no value. A cure for rabies is as yet undiscovered; but the Pasteur treatment is effective in preventing the development of the disease in persons bitten by rabid animals.

DOSAGE: The antirabic treatment consists of the injection of 25 doses of Rabies Vaccine, prepared after the method of Pasteur; the injections being given daily for 21 successive days.

METHOD OF ADMINISTRATION: After painting the skin with iodine, the injections are given into the subcutaneous tissues of the anterior abdominal wall. The entire amount in each vial should be administered at a single injection. Each subsequent injection should be made in a widely distant area of tissue, and with a freshly sterilized syringe and needle, using vaccine in vial next in order numerically. No after-treatment of the site of injection is required.

CONTAINERS: Lederle's Rabies Vaccine is marketed in the Lederle Vial, with soft rubber stopper which can be easily punctured with the needle of an ordinary hypodermic syringe.

PACKAGES: For styles of packages, see price-list.

Small-Pox

HISTORICAL: Small-pox is fatal to a very large proportion of those whom it attacks. It kills from 30 to 40 per cent of its victims. The history of this loathsome disease can be traced back many centuries before Christ, always and in every way adding to the burden of human misery; attributed sometimes to the wrath of God and sometimes to the malignant condition of the atmosphere. It was spread by war, by the great Crusades, by religious pilgrimages, and by commercial caravans. In the second, sixth, eleventh and twelfth centuries, it ravaged Europe exacting a death toll of from 40 to 70 per cent among

primitive races, reaching its zenith in the eighteenth century. At this time, 10 per cent of the total mortality in England was due to small-pox and one person in every five was horribly scarred. In Prussia, there were 25,000 deaths annually, and in France, 30,000. Following the discovery of Jenner, however, a rapid decrease in both morbidity and mortality as well as in the territorial extent of small-pox was noted.

RESULTS OF VACCINATION: Professor Councilman of Harvard University remarked: "It is impossible to overestimate the influence which it has exercised in furthering civilization and the physical and moral advance of the human race. Without vaccination and with the present inter-communication, small-pox would be pandemic raging over the entire world."

Of the millions of immigrants arriving at Ellis Island each year, every one is vaccinated en route and rarely indeed with untoward consequences. Cuba with compulsory vaccination laws has not registered a case of small-pox since 1902. In observations made for 21 years on 4,000,000 people in Bohemia, it was discovered that the death rate among vaccinated persons was 5 per cent, while among those who had never been vaccinated, it was 29 per cent. Illustrations of this kind could be multiplied as almost countless authentic statistics exist.

TECHNIQUE OF VACCINATION: Trivial and simple as the operation of vaccination appears, it is nevertheless a surgical procedure and one requiring skill and

special knowledge to secure the most successful and satisfactory results. Moreover, the after-care of the wound is exceedingly important.

The hands of the operator, the instrument used and the site of vaccination should be clean. In preparing the site of inoculation, use soap and water and dry with a clean towel. Alcohol may be used in addition, if allowed to evaporate before proceeding with the operation; otherwise the antiseptic may easily destroy the life of the virus. Two or three linear scarifications about one-sixteenth of an inch long should be made with a sterile instrument; the scarifications should not penetrate the subcutaneous tissue, for, if profuse bleeding occurs, any virus which is rubbed into such a scarified area would be washed away by the bleeding. Avoid large scarifications as they easily become infected and lead to complications. Rub the virus slowly and thoroughly into the scarified area, remembering that it requires time to properly perform this portion of the operation. Let the serum on scarified area dry before the clothing is replaced. Protect the vaccination from contamination by a piece of sterile gauze; but under no circumstances use shields which cover the part closely—for the circulation is thereby constricted, inspection of the part prevented, and the application of proper dressings rendered impossible. Supervision and proper after-care will prevent complications. An infected vaccination should be promptly cleaned out and treated on general surgical principles like any other infected wound.

PREPARATION: All Vaccine Virus prepared by the Lederle Antitoxin Laboratories is made under U. S. Government license in strict compliance with the regulations of the Public Health and Marine Hospital Service, and is subjected to the following tests:

(1) Careful bacteriologic study is made of the green virus, especial attention being given to searching for the possibility of the presence of tetanus organisms.

(2) The purity and safety of the finished product are established by further bacteriologic study and by animal inoculations.

(3) The Lederle Antitoxin Laboratories also test each lot of Vaccine Virus physiologically on children before placing it upon the market; this being the only absolute test of activity that can be applied.

CONTAINERS: Lederle's Glycerinated Vaccine Virus is supplied in soft wax tubes and in glass capillary tubes.

PACKAGES: For styles of packages, see price-list.

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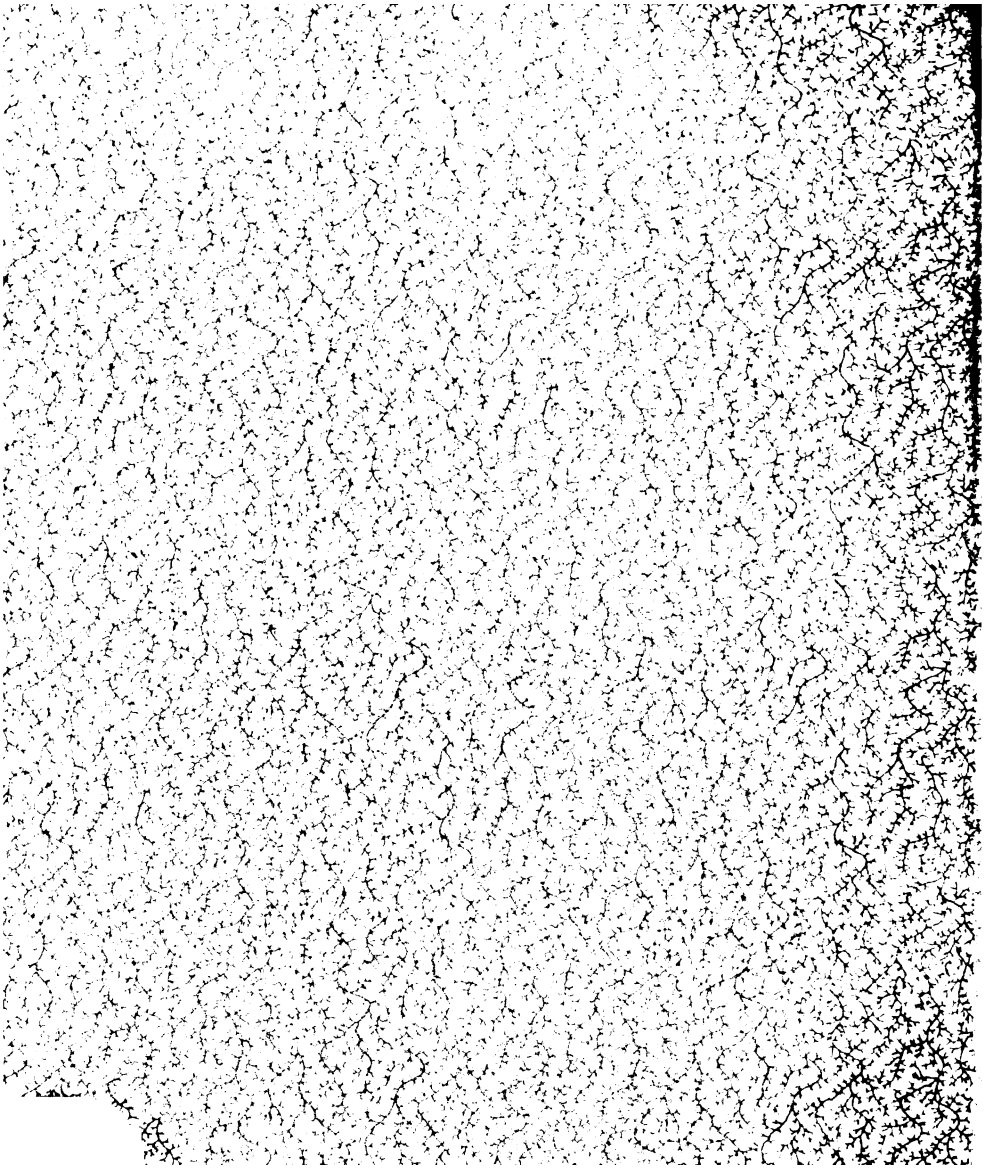

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the horse manure is generally infected, as the tetanus bacilli grow in the intestines of this animal and the spores remain alive in the dirt for years. In cases where the wounds are extensive and it is impossible to thoroughly clean the wounds, it is advisable to give a second prophylactic injection of antitoxin at the end of ten days. TETANUS ANTITOXIN is used both as a prophylactic and therapeutic agent. TETANUS ANTITOXIN is almost an absolute specific against the development of tetanus, when given within 12 or 24 hours after the injury.

METHOD OF ADMINISTRATION: As a prophylactic. Tetanus Antitoxin is usually given subcutaneously at any point where there is sufficient subcutaneous tissue. By this method, the antitoxin is given out into the circulation slowly, and is not, therefore, eliminated rapidly; so that the immunity will persist for the maximum period. In cases where the wound has been neglected for several days, however, it is better to administer the antitoxin as near to the wound as possible, so as to flood the tissues in the immediate vicinity; and the injection should be deep, intra-muscular if possible, so as to permit its rapid absorption by the motor nerves. If any nerves are exposed in the wound, the antitoxin should be injected into them. It appears to be a well-ascertained fact that most of the antitoxin is eliminated from the system in about 8 or 10 days after the injection; hence, it is advisable to administer a second prophylactic dose at

the end of 8 or 10 days, in order to maintain the immunity induced by the first injection.

For curative use, four methods of administration of Tetanus Antitoxin are advocated: namely, subcutaneous, intravenous, intraspinal and intraneural.

1. Subcutaneous Injection. This is the method which has been usually employed, but the reports are not encouraging. If administered in this way, the antitoxin is absorbed by the lymphatics, transported to the veins, passes through the lungs and finally is distributed through the arterial system to all parts of the body. Only a very small dose ultimately reaches the motor nerves, through which the toxin is being carried to the spinal cord, while by far the greater part of the antitoxin is distributed to the viscera, where it can be of no possible use.

2. Tetanus Antitoxin administered only by the intravenous method is not very effective; the amount required by this route to produce any therapeutic effect is enormous, as is proved by the observation of various investigators.

3. Intraspinal Injection. Experimentally, treatment of tetanus by intraspinal injections of tetanus antitoxin has not been very encouraging, but much more satisfactory results have been obtained in actual practice.

4. Intraneural Injection. This method was first employed clinically by Kuester in 1902. As it is a well-ascertained fact that most and possibly all of the toxin reaches the spinal cord only by traveling up its nerves, it is

theoretically logical to inject the antitoxin into the nerves in order that, like the toxin, it may reach the spinal cord by the easiest route. That it will do this, when injected intraneurally, admits of no doubt, in view of the overwhelming experimental evidence on this point. Just how the antitoxin acts, and by which intraneural route it reaches the cord, has not been determined. The only possible methods for reaching all the nerves at once are (1) intravenous injections, and (2) intraspinal injections. In no case, therefore, should the surgeon depend on intraneural injections alone, and in no case should he omit either intraspinal injections or injections into the motor nerves leading from the site of inoculation, or intravenous injections. In the patients who have recovered after this form of treatment, no disability appears to have been caused.

Regardless of the method of administration, the most important thing in the treatment is to give the maximum quantity of antitoxin indicated as soon as possible, for delay, even of a few hours, may mean a fatal result. It is desirable for the entire amount of antitoxin to be administered at one time and as soon as possible after diagnosis has been made.

DOSAGE: For Immunization: The immunizing dose agreed upon by a committee of American Bacteriologists as sufficient to protect against the development of tetanus within the incubation period is 1,500 units of American standard. For Curative Treatment: If the

injections are given subcutaneously, 100,000 units will be required in the first 24 hours for the usual acute type of case in an adult, and although a smaller amount may be sufficient for a child or for an apparently mild case, one cannot be sure of that fact, and it is better to give too much than too little. If administered intravenously, probably 20,000 to 40,000 units should be administered at first and repeated after the lapse of 18 to 24 hours. If given intraspinally, from 3,000 to 10,000 units should be given according to the severity of the case, and this dose need not, as a rule, be repeated in less than 18 or 24 hours. If given intraneurally, injections of antitoxin should be made in as great amount as the nerve-sheaths will contain; for example, 1,500 units in the sciatic nerve and 750 units in the anterior crural or obturator nerves. If the injections are made slowly, practically all of this quantity can be introduced among the nerve fibers.

The most logical antitoxic treatment of tetanus is to administer the antitoxin intraspinally and intravenously in all cases; and intraneural injections should be made whenever possible.

QUANTITY IN CONTAINER: Refined and concentrated Tetanus Antitoxin is supplied by the Lederle Antitoxin Laboratories in the following strengths: 1,500, 3,000 and 5,000 units.

PREPARATION: In 1905, the Research Laboratories of the Department of Health of New York City perfected a practical method for separating diphtheria

antitoxin in a refined and concentrated form from the blood serum of an immunized horse. In 1907, the Lederle Antitoxin Laboratories introduced to the medical profession the refined and concentrated tetanus antitoxin product, prepared by the method outlined by Robert B. Gibson and employed in the preparation of Lederle's Diphtheria Antitoxin, as described on page 37.

CONTAINERS: See page 70.

PACKAGES: For styles of packages, see price-list.

Typhoid Fever

(Prophylaxis and Treatment)

TYPHOID VACCINE (PROPHYLACTIC) is now employed as an immunizing agent in all the important armies of the world. In the United States Army and Navy, all officers and enlisted men under 45 years of age are immunized against typhoid fever. Realizing the tremendous saving and the benefit derived from prophylactic immunization against typhoid fever, many corporations, where large numbers of men are employed, are now recommending typhoid inoculation to the employees.

In the treatment of typhoid fever, no single remedy has proven of such value as TYPHOID VACCINE. Very encouraging results are constantly being reported; the fever becomes milder and of shorter duration; fewer relapses occur; and complications are lessened.

PARATYPHOID FEVER, being very similar to typhoid, is frequently confused with it. Clinically, this disease resembles typhoid fever, but usually follows a mild course. By careful technique, many cases of fevers now classed as "undetermined" may possibly be found to be paratyphoid. TYPHOID COMBINED VACCINE is now coming into general use as an immunizing agent against paratyphoid fever, as well as against typhoid fever, inasmuch as this vaccine contains both the typhoid and paratyphoid bacilli.

DOSAGE: As an immunizing agent, TYPHOID VACCINE (PROPHYLACTIC) is administered in three doses at intervals of ten days; an initial dose of 500 million is followed by two successive doses of 1,000 million each. The first immunizing dose sometimes produces headache, malaise, slight fever, and tenderness and redness about the site of the inoculation; but these symptoms pass off at the end of 24 to 48 hours.

In the treatment of typhoid fever, very encouraging results are constantly being reported with TYPHOID VACCINE. At first, the therapeutic dose consisted of 25 million administered every second day; but lately, better results seem to be achieved by giving 300 million as the initial dose and increasing 100 million every second or third day until 1,000 million are given at a dose. The vaccine treatment ought to be given as soon as a diagnosis is made, and should be continued until the temperature becomes normal.